

=> s (9002-06-6 OR 4408-78-0 OR 4428-95-9 OR 59277-89-3 OR 66341-16-0 OR 82410-32-0 OR 86761-39-9 OR 104227-87-4 OR 106941-25-7 OR 113852-37-2 OR 161363-19-5 OR 123994-68-3 OR 59-23-4 OR 9000-01-5)/rn

6484 9002-06-6
 75 9002-06-6D
 6415 9002-06-6/RN
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 648 4408-78-0
 47 4408-78-0D
 613 4408-78-0/RN
 (4408-78-0 (NOTL) 4408-78-0D)
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 54 4428-95-9D
 999 4428-95-9/RN
 (4428-95-9 (NOTL) 4428-95-9D)
 3559 59277-89-3
 161 59277-89-3D
 3443 59277-89-3/RN
 (59277-89-3 (NOTL) 59277-89-3D)
 68 66341-16-0
 12 66341-16-0D
 62 66341-16-0/RN
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 3175 82410-32-0
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 535 104227-87-4/RN
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 27 106941-25-7D
 631 106941-25-7/RN
 (106941-25-7 (NOTL) 106941-25-7D)
 687 113852-37-2
 28 113852-37-2D
 668 113852-37-2/RN
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 11 161363-19-5
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113852-37-2 OR 161363-19-5 OR 123994-68-3 OR 59-23-4 OR 9000-01-5)/RN

=> s (9002-89-5 OR 9004-34-6 OR 9005-25-8 OR 9012-36-6 OR 24980-41-4 OR 25248-42-4 OR 26023-30-3 OR 26063-00-3 OR 26100-51-6 OR 26744-04-7 OR 26913-47-3 OR 28158-18-1 OR 28803-92-1 OR 34346-01-5 OR 90409-78-2 OR 121065-55-2 OR 718636-43-2)/rn

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 26744-04-7 OR 26913-47-3 OR 28158-18-1 OR 28803-92-1 OR 34346-01-
 5 OR 90409-78-2 OR 121065-55-2 OR 718636-43-2)/RN

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(FILE 'HOME' ENTERED AT 15:58:27 ON 02 MAY 2007)

FILE 'HCAPLUS' ENTERED AT 15:58:36 ON 02 MAY 2007
 E US20040259832/PN 25

L1 1 S E3

FILE 'STNGUIDE' ENTERED AT 15:59:26 ON 02 MAY 2007

FILE 'HCAPLUS' ENTERED AT 16:02:09 ON 02 MAY 2007

L2 43567 S (9002-06-6 OR 4408-78-0 OR 4428-95-9 OR 59277-89-3 OR 66341-
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=> s l2 or l3

L4 276194 L2 OR L3

=> s l4 and l1

L5 1 L4 AND L1

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L5 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:681513 HCAPLUS <<LOGINID::20070502>>

DOCUMENT NUMBER: 141:185078

TITLE: Novel antiherpes drug combinations of Herpes simplex
 virus thymidine kinase inhibitors and antiherpes
 substances

INVENTOR(S): Wright, George E.

PATENT ASSIGNEE(S): University of Massachusetts, USA

SOURCE: PCT Int. Appl., 22 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004069168	A2	20040819	WO 2004-US2427	20040129
WO 2004069168	A3	20050915		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,			
	CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,			
	GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,			
	LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI			
RW:	BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE,			
	BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU,			

MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN,
GQ, GW, ML, MR, NE, SN, TD, TG

CA 2514334 A1 20040819 CA 2004-2514334 20040129
US 2004259832 A1 20041223 US 2004-767019 20040129 <--
EP 1594507 A2 20051116 EP 2004-706459 20040129

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

PRIORITY APPLN. INFO.:

US 2003-443519P P 20030129
WO 2004-US2427 W 20040129

AB Composition and methods are disclosed that include a synergistic combination of
an inhibitor of Herpes simplex virus thymidine kinase, and an antiherpes
substance. The effect of combination of 2-phenylamino-9-(4-hydroxybutyl)-
6-oxopurine and foscarnet against HSV2 encephalitis in mice was examined

IT 9002-06-6, Thymidine kinase

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Herpes simplex virus; antiherpes drug combinations of Herpes simplex
virus thymidine kinase inhibitors and antiherpes substances)

RN 9002-06-6 HCAPLUS

CN Kinase (phosphorylating), thymidine (CA INDEX NAME)

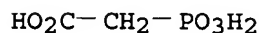
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IT 4408-78-0 4428-95-9, Foscarnet 59277-89-3,
Acyclovir 66341-16-0, Acyclovir monophosphate 82410-32-0
, Ganciclovir 86761-39-9 104227-87-4, Famciclovir
106941-25-7, PMEA 113852-37-2, Cidofovir
161363-19-5

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(antiherpes drug combinations of Herpes simplex virus thymidine kinase
inhibitors and antiherpes substances)

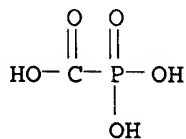
RN 4408-78-0 HCAPLUS

CN Acetic acid, 2-phosphono- (CA INDEX NAME)



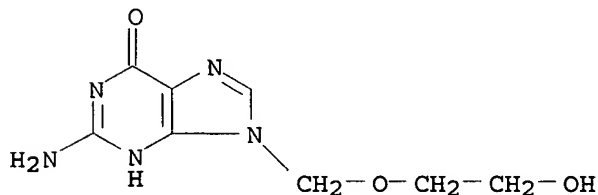
RN 4428-95-9 HCAPLUS

CN Phosphinecarboxylic acid, 1,1-dihydroxy-, 1-oxide (CA INDEX NAME)



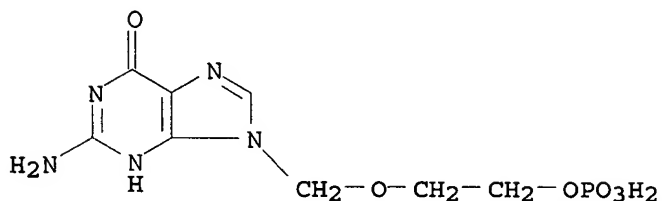
RN 59277-89-3 HCAPLUS

CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[(2-hydroxyethoxy)methyl]- (CA
INDEX NAME)



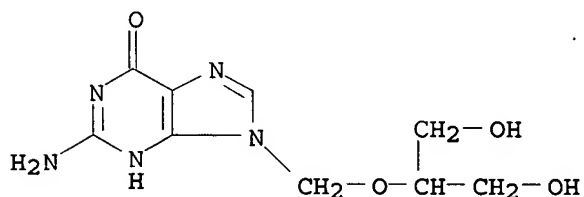
RN 66341-16-0 HCAPLUS

CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[[2-(phosphonoxy)ethoxy)methyl] - (CA INDEX NAME)



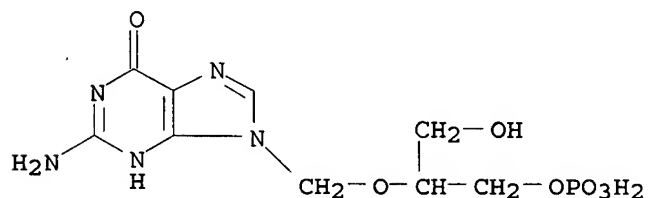
RN 82410-32-0 HCAPLUS

CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[[2-hydroxy-1-(hydroxymethyl)ethoxy)methyl] - (CA INDEX NAME)



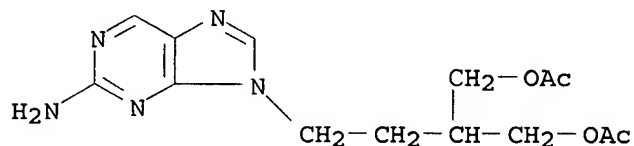
RN 86761-39-9 HCAPLUS

CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[[1-(hydroxymethyl)-2-(phosphonoxy)ethoxy)methyl] - (CA INDEX NAME)



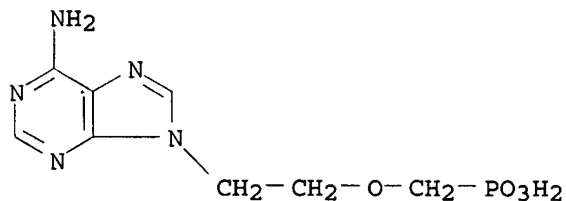
RN 104227-87-4 HCAPLUS

CN 1,3-Propanediol, 2-[2-(2-amino-9H-purin-9-yl)ethyl] -, 1,3-diacetate (CA INDEX NAME)



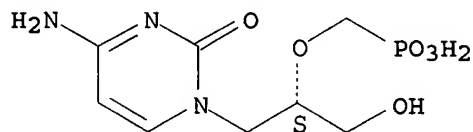
RN 106941-25-7 HCAPLUS

CN Phosphonic acid, P-[[2-(6-amino-9H-purin-9-yl)ethoxy)methyl] - (CA INDEX NAME)

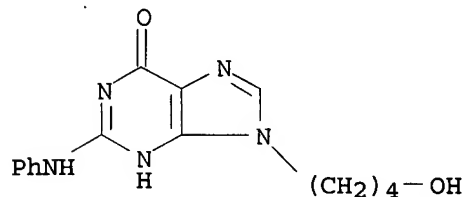


RN 113852-37-2 HCAPLUS
 CN Phosphonic acid, P-[[[(1S)-2-(4-amino-2-oxo-1(2H)-pyrimidinyl)-1-(hydroxymethyl)ethoxy]methyl]- (CA INDEX NAME)

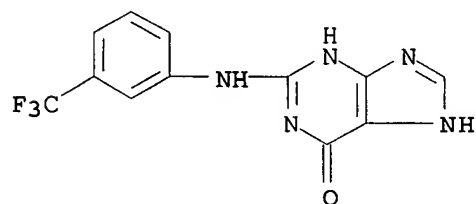
Absolute stereochemistry.



RN 161363-19-5 HCAPLUS
 CN 6H-Purin-6-one, 1,9-dihydro-9-(4-hydroxybutyl)-2-(phenylamino)- (9CI) (CA INDEX NAME)



IT 123994-68-3
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (antiherpes drug combinations of Herpes simplex virus thymidine kinase inhibitors and antiherpes substances)
 RN 123994-68-3 HCAPLUS
 CN 6H-Purin-6-one, 1,7-dihydro-2-[[3-(trifluoromethyl)phenyl]amino]- (9CI) (CA INDEX NAME)



IT 59-23-4, Galactose, biological studies 9000-01-5, Gum
 arabic 9002-89-5, Polyvinylalcohol 9004-34-6,
 Cellulose, biological studies 9005-25-8, Starch, biological
 studies 9012-36-6, Agarose 24980-41-4,

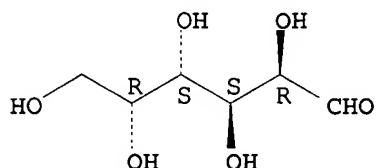
Polycaprolactone 25248-42-4, Polycaprolactone 26023-30-3
 , Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)] 26063-00-3,
 Polyhydroxybutyrate 26100-51-6, Lactic acid homopolymer
 26744-04-7 26913-47-3, Poly[oxy(1,10-dioxo-1,10-
 decanediyl)] 28158-18-1 28803-92-1 34346-01-5
 , Lactic acid-glycolic acid copolymer 90409-78-2,
 1,3-Bis(carboxyphenoxypropane)-sebacic acid copolymer 121065-55-2
 718636-43-2

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (antiherpes drug combinations of Herpes simplex virus thymidine kinase
 inhibitors and antiherpes substances and carriers)

RN 59-23-4 HCAPLUS

CN D-Galactose (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 9000-01-5 HCAPLUS

CN Gum arabic (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

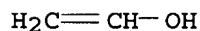
RN 9002-89-5 HCAPLUS

CN Ethenol, homopolymer (CA INDEX NAME)

CM 1

CRN 557-75-5

CMF C2 H4 O



RN 9004-34-6 HCAPLUS

CN Cellulose (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 9005-25-8 HCAPLUS

CN Starch (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 9012-36-6 HCAPLUS

CN Agarose (CA INDEX NAME)

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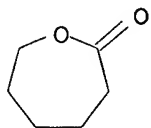
RN 24980-41-4 HCAPLUS

CN 2-Oxepanone, homopolymer (CA INDEX NAME)

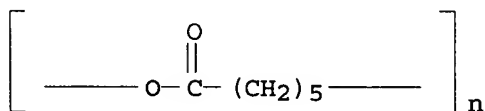
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CRN 502-44-3

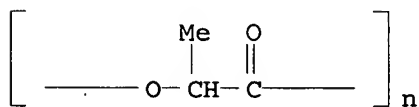
CMF C6 H10 O2



RN 25248-42-4 HCAPLUS
CN Poly[oxy(1-oxo-1,6-hexanediyl)] (CA INDEX NAME)



RN 26023-30-3 HCAPLUS
CN Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)] (CA INDEX NAME)

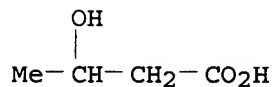


RN 26063-00-3 HCAPLUS
CN Butanoic acid, 3-hydroxy-, homopolymer (CA INDEX NAME)

CM 1

CRN 300-85-6

CMF C4 H8 O3

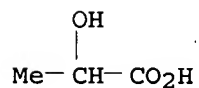


RN 26100-51-6 HCAPLUS
CN Propanoic acid, 2-hydroxy-, homopolymer (CA INDEX NAME)

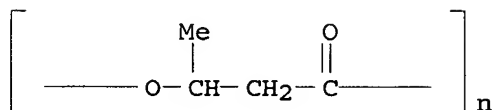
CM 1

CRN 50-21-5

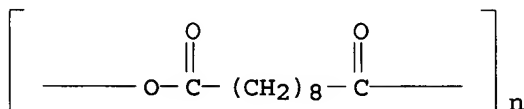
CMF C3 H6 O3



RN 26744-04-7 HCAPLUS
CN Poly[oxy(1-methyl-3-oxo-1,3-propanediyl)] (CA INDEX NAME)



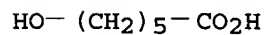
RN 26913-47-3 HCAPLUS
 CN Poly[oxy(1,10-dioxo-1,10-decanediyl)] (CA INDEX NAME)



RN 28158-18-1 HCAPLUS
 CN Hexanoic acid, 6-hydroxy-, homopolymer (CA INDEX NAME)

CM 1

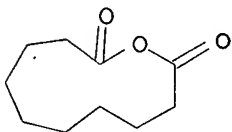
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RN 28803-92-1 HCAPLUS
 CN Oxacycloundecane-2,11-dione, homopolymer (CA INDEX NAME)

CM 1

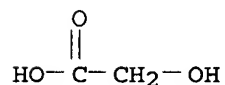
CRN 2561-88-8
 CMF C10 H16 O3



RN 34346-01-5 HCAPLUS
 CN Propanoic acid, 2-hydroxy-, polymer with 2-hydroxyacetic acid (CA INDEX NAME)

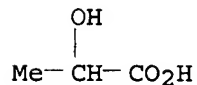
CM 1

CRN 79-14-1
 CMF C2 H4 O3



CM 2

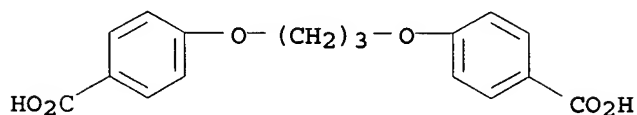
CRN 50-21-5
CMF C3 H6 O3



RN 90409-78-2 HCAPLUS
CN Decanedioic acid, polymer with 4,4'-[1,3-propanediylbis(oxy)]bis[benzoic acid] (CA INDEX NAME)

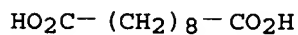
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CRN 3753-81-9
CMF C17 H16 O6



CM 2

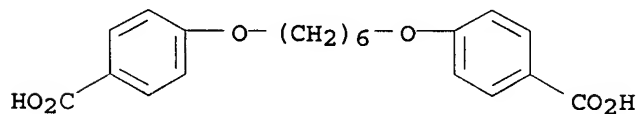
CRN 111-20-6
CMF C10 H18 O4



RN 121065-55-2 HCAPLUS
CN Decanedioic acid, polymer with 4,4'-[1,6-hexanediylbis(oxy)]bis[benzoic acid] (CA INDEX NAME)

CM 1

CRN 74774-53-1
CMF C20 H22 O6



CM 2

CRN 111-20-6

10767019>05/05/2007

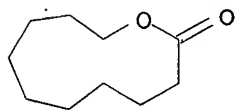
CMF C10 H18 O4

HO₂C- (CH₂)₈- CO₂H

RN 718636-43-2 HCAPLUS
CN Oxacycloundecan-2-one, homopolymer (9CI) (CA INDEX NAME)

CM 1

CRN 5579-79-3
CMF C10 H18 O2



=>

=> fil stng

COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
13.07	17.70

FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE	TOTAL
ENTRY	SESSION
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FILE 'STNGUIDE' ENTERED AT 16:03:41 ON 02 MAY 2007
USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT
COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY, JAPAN SCIENCE
AND TECHNOLOGY CORPORATION, AND FACHINFORMATIONSZENTRUM KARLSRUHE

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Apr 27, 2007 (20070427/UP).

=> d his

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FILE 'HCAPLUS' ENTERED AT 15:58:36 ON 02 MAY 2007
E US20040259832/PN 25

L1 1 S E3

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FILE 'HCAPLUS' ENTERED AT 16:02:09 ON 02 MAY 2007

L2 43567 S (9002-06-6 OR 4408-78-0 OR 4428-95-9 OR 59277-89-3 OR 66341-
L3 237600 S (9002-89-5 OR 9004-34-6 OR 9005-25-8 OR 9012-36-6 OR 24980-4
L4 276194 S L2 OR L3
L5 1 S L4 AND L1

FILE 'STNGUIDE' ENTERED AT 16:03:41 ON 02 MAY 2007

=> fil hcaplus

10767019>05/05/2007

COST IN U.S. DOLLARS	SINCE FILE	TOTAL
FULL ESTIMATED COST	ENTRY	SESSION
	0.42	18.12
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
CA SUBSCRIBER PRICE	ENTRY	SESSION
	0.00	-0.78

FILE 'HCAPLUS' ENTERED AT 16:07:58 ON 02 MAY 2007
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FILE COVERS 1907 - 2 May 2007 VOL 146 ISS 19
FILE LAST UPDATED: 1 May 2007 (20070501/ED)

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This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s (59277-89-3 OR 66341-16-0 OR 82410-32-0 OR 86761-39-9 OR 104227-87-4 OR 106941-25-7 OR 113852-37-2 OR 161363-19-5 OR 123994-68-3)/rn
3559 59277-89-3
161 59277-89-3D
3443 59277-89-3/RN
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68 66341-16-0
12 66341-16-0D
62 66341-16-0/RN
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(104227-87-4 (NOTL) 104227-87-4D)
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631 106941-25-7/RN
(106941-25-7 (NOTL) 106941-25-7D)
687 113852-37-2
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668 113852-37-2/RN
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      )/RN

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    278618 "INFECTION"
      80491 "INFECTIONS"
    317344 "INFECTION"
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      26185 "HERPES"
      9531 "INFECTION" (L) "HERPES"
    255359 "SKIN"
      10347 "SKINS"
    261228 "SKIN"
        ("SKIN" OR "SKINS")
      950108 "DISEASE"
      257279 "DISEASES"
    1065303 "DISEASE"
        ("DISEASE" OR "DISEASES")
      32833 "SKIN, DISEASE"
        ("SKIN" (W) "DISEASE")
      26185 "HERPES"
      489 "SKIN, DISEASE" (L) "HERPES"
L7    2471 L6 AND (HERPES OR "HERPES" OR "INFECTION" (L) "HERPES" OR "SKIN,
      DISEASE" (L) "HERPES")

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=> d 17 ibib abs hitstr

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L7    ANSWER 1 OF 2471  HCAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:      2007:268504  HCAPLUS <<LOGINID::20070502>>
DOCUMENT NUMBER:       146:386676
TITLE:                 Effects of bicistronic lentiviral vector-mediated
                        herpes simplex virus thymidine
                        kinase/ganciclovir system on human lens epithelial
                        cells
AUTHOR(S):             Yang, Jin; Liu, Tian Jin; Lu, Yi
CORPORATE SOURCE:      Department of Ophthalmology, Eye and ENT Hospital,
                        Fudan University, Shanghai, Peop. Rep. China
SOURCE:                Current Eye Research (2007), 32(1), 33-42
                        CODEN: CEYRDM; ISSN: 0271-3683
PUBLISHER:             Taylor & Francis, Inc.
DOCUMENT TYPE:         Journal
LANGUAGE:              English
AB    Posterior capsule opacification (PCO) is the most common complication
      after phacoemulsification cataract surgery. Hyperplasia of the lens
      epithelial cell after phacoemulsification is thought to be an important
      feature contributing to PCO. In this study, we investigated the
      feasibility of killing the human lens epithelial cells (HLECs) by
      lentivirus-mediated herpes simplex virus thymidine kinase
      (HSV-tk) gene/ganciclovir (GCV) in HLECs and studied the bystander effect.
      HLECs were infected with lentiviral vectors coexpressing HSV-tk and
      enhanced green fluorescent protein (EGFP) or expressing EGFP alone and
      treated with ganciclovir. Infection efficiency was assessed by
      fluorescence microscopy, fluorescence-activated cell sorting, and reverse

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transcription PCR. The cytotoxicity of the HSV-tk/GCV suicide gene therapy system was assessed by DNA ladder and electron microscopy. The time effect and bystander effect of HLEC growth inhibition were evaluated with cell proliferation assay. Lentiviral vector-mediated stable integration and efficient expression of HSV-tk in HLECs, with infection efficiency exceeding 95% GCV at concns. of 15. apprx. 25 µg/mL, significantly induced apoptosis or necrosis of infected HLECs. GCV also killed normal cells mixed with HSV-tk infected cells. The bystander effect markedly increased the cytotoxicity of the HSV-tk/GCV system. Our results suggest that bicistronic lentiviral vectors can efficiently integrate several genes into HLECs and may be a gene therapy platform. Lentivirus-mediated suicide gene therapy might be a feasible treatment strategy to prevent capsule opacification.

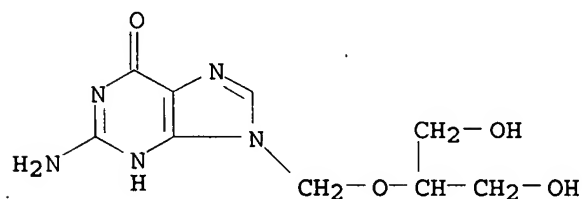
IT 82410-32-0, Ganciclovir

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(bicistronic lentiviral vector-mediated herpes simplex virus thymidine kinase/ganciclovir system exhibit higher cytotoxicity levels suggest that it can efficiently integrate several genes in human lens epithelial cells)

RN 82410-32-0 HCAPLUS

CN 6H-Purin-6-one; 2-amino-1,9-dihydro-9-[[2-hydroxy-1-(hydroxymethyl)ethoxy]methyl]- (CA INDEX NAME)



REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> s acyclovir ?phosphate?

3855 ACYCLOVIR

841237 ?PHOSPHATE?

L8 113 ACYCLOVIR ?PHOSPHATE?

(ACYCLOVIR(W) ?PHOSPHATE?)

=> s 18 and 17

L9 40 L8 AND L7

=> d 19 ibib abs hitstr

L9 ANSWER 1 OF 40 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2007:150707 HCAPLUS <<LOGINID::20070502>>

DOCUMENT NUMBER: 146:198656

TITLE: Methods for treating or preventing reactivation of a latent herpesvirus infection

INVENTOR(S): Schaffer, Priscilla; Bringham, Ryan

PATENT ASSIGNEE(S): Beth Israel Deaconess Medical Center, USA

SOURCE: PCT Int. Appl., 83pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007016450	A2	20070208	WO 2006-US29663	20060731
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

PRIORITY APPLN. INFO.:

US 2005-703835P

P 20050729

AB The invention is directed to methods and compns. for treating or preventing reactivation of a latent herpesvirus infection and the associated complications and outcomes. The methods involve administering a composition comprising glutamine, or a derivative, conjugate, or analog thereof.

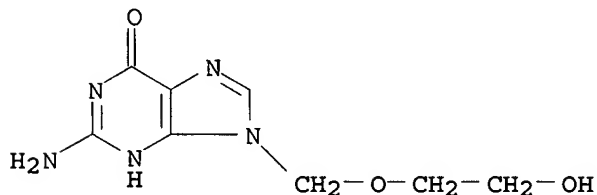
IT 59277-89-3, Acyclovir 66341-16-0, Acyclovir monophosphate 82410-32-0, Ganciclovir 86761-39-9
 104227-87-4, Famciclovir 106941-25-7, PMEA
 113852-37-2, Cidofovir

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(methods for treating or preventing reactivation of a latent herpesvirus infection using glutamine and its analogs in combination with other agents)

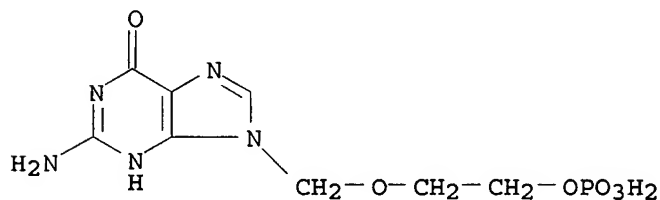
RN 59277-89-3 HCAPLUS

CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[(2-hydroxyethoxy)methyl]- (CA INDEX NAME)



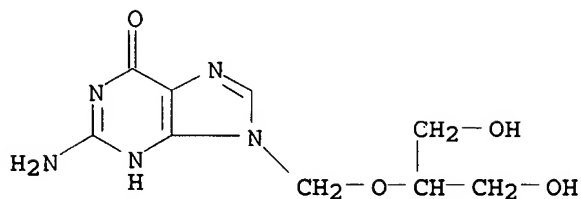
RN 66341-16-0 HCAPLUS

CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[[2-(phosphonoxy)ethoxy]methyl]- (CA INDEX NAME)

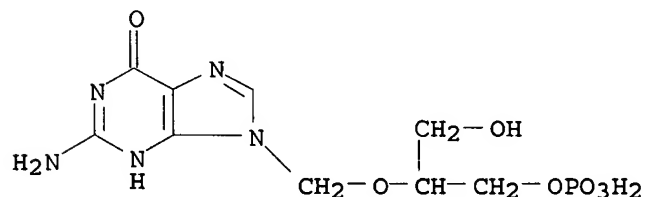


RN 82410-32-0 HCAPLUS

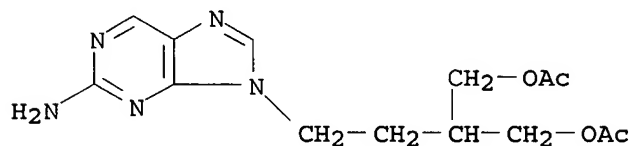
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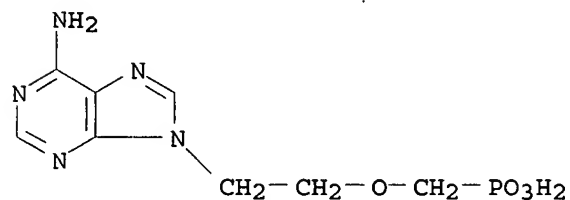
RN 86761-39-9 HCAPLUS
 CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[[1-(hydroxymethyl)-2-(phosphonoxy)ethoxy]methyl]- (CA INDEX NAME)



RN 104227-87-4 HCAPLUS
 CN 1,3-Propanediol, 2-[2-(2-amino-9H-purin-9-yl)ethyl]-, 1,3-diacetate (CA INDEX NAME)

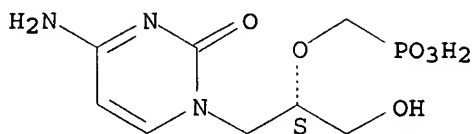


RN 106941-25-7 HCAPLUS
 CN Phosphonic acid, P-[[2-(6-amino-9H-purin-9-yl)ethoxy]methyl]- (CA INDEX NAME)



RN 113852-37-2 HCAPLUS
 CN Phosphonic acid, P-[[[(1S)-2-(4-amino-2-oxo-1(2H)-pyrimidinyl)-1-(hydroxymethyl)ethoxy]methyl]- (CA INDEX NAME)

Absolute stereochemistry.



=> d his

(FILE 'HOME' ENTERED AT 15:58:27 ON 02 MAY 2007)

FILE 'HCAPLUS' ENTERED AT 15:58:36 ON 02 MAY 2007
E US20040259832/PN 25

L1 1 S E3

FILE 'STNGUIDE' ENTERED AT 15:59:26 ON 02 MAY 2007

FILE 'HCAPLUS' ENTERED AT 16:02:09 ON 02 MAY 2007

L2 43567 S (9002-06-6 OR 4408-78-0 OR 4428-95-9 OR 59277-89-3 OR 66341-
L3 237600 S (9002-89-5 OR 9004-34-6 OR 9005-25-8 OR 9012-36-6 OR 24980-4
L4 276194 S L2 OR L3
L5 1 S L4 AND L1

FILE 'STNGUIDE' ENTERED AT 16:03:41 ON 02 MAY 2007

FILE 'HCAPLUS' ENTERED AT 16:07:58 ON 02 MAY 2007

L6 6746 S (59277-89-3 OR 66341-16-0 OR 82410-32-0 OR 86761-39-9 OR 104
E HERPES+ALL/CT
L7 2471 S L6 AND (HERPES OR "HERPES" OR "INFECTION" (L) "HERPES" OR "SK
L8 113 S ACYCLOVIR ?PHOSPHATE?
L9 40 S L8 AND L7

=> S L9 AND 1800<=PY<=2003

23932189 1800<=PY<=2003

L10 38 L9 AND 1800<=PY<=2003

=> d l10 ibib abs hitstr

L10 ANSWER 1 OF 38 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:153908 HCAPLUS <<LOGINID::20070502>>

DOCUMENT NUMBER: 137:338

TITLE: Antiviral activity of cyclosaligenyl prodrugs of acyclovir, carbovir, and abacavir

AUTHOR(S): Balzarini, Jan; Haller-Meier, Friederike; De Clercq, Erik; Meier, Chris

CORPORATE SOURCE: Rega Institute for Medical Research, KU Leuven, Louvain, Belg.

SOURCE: Antiviral Chemistry & Chemotherapy (2001), 12(5), 301-306

CODEN: ACCHEH; ISSN: 0956-3202

PUBLISHER: International Medical Press

DOCUMENT TYPE: Journal

LANGUAGE: English

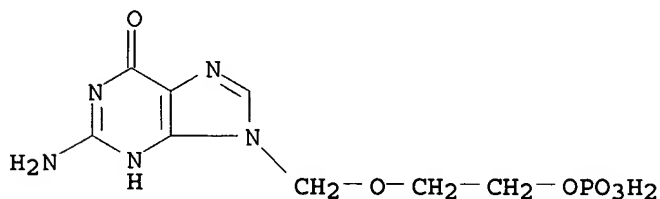
AB The cyclosaligenyl (cycloSal) derivs. of the monophosphates of 3 acyclic or carbocyclic guanosine analogs, for example, acyclovir (ACV), carbovir (CBV), and abacavir (ABC), were investigated for their activity against retrovirus (HIV, Moloney sarcoma virus) and herpes simplex virus (HSV) activity in cell culture. The extent of the antiviral potency of the prodrugs depended on the nature of the nucleoside, the substituent on the cycloSal moiety and the virus investigated. Most notably, and unlike

the parent compound ACV, cycloSal-ACV monophosphate (MP) prodrugs retained pronounced activity against ACV-resistant (thymidine kinase-deficient) HSV-1 and also gained anti-HIV activity. While the cycloSal-CBVMP prodrugs did not show enhanced activity compared with the parent compound CBV, the cycloSal-ABCMP prodrugs afforded markedly increased potency against both HSV and HIV. The authors' data indicate that the cycloSal prodrug approach can be useful to deliver directly the MP derivs. of nucleoside analogs into the intact, virus-infected cells, thus improving and extending the antiviral potency and spectrum of the drugs against retro- and herpesvirus strains.

IT 66341-16-0, Acyclovir monophosphate
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (cyclosaligenyl prodrugs; antiviral activity of cyclosaligenyl prodrugs of acyclovir, carbovir, and abacavir)

RN 66341-16-0 HCAPLUS

CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[[2-(phosphonoxy)ethoxy)methyl] - (CA INDEX NAME)



REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d l10 ibib abs hitstr 2-10

L10 ANSWER 2 OF 38 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:580763 HCAPLUS <<LOGINID::20070502>>

DOCUMENT NUMBER: 135:327001

TITLE: The potency of acyclovir can be markedly different in different cell types

AUTHOR(S): Brandi, Giorgio; Schiavano, Giuditta F.; Balestra, Emanuela; Tavazzi, Barbara; Perno, Carlo-Federico; Magnani, Mauro

CORPORATE SOURCE: Institute of Toxicologic Hygienic and Environmental Science, "G. Fornaini" University of Urbino, Urbino, Italy

SOURCE: Life Sciences (2001), 69(11), 1285-1290
 CODEN: LIFSAK; ISSN: 0024-3205

PUBLISHER: Elsevier Science Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Acyclovir is an acyclic guanine analog with a considerable activity against herpes simplex viruses. We studied the antiherpetic activity of acyclovir in macrophages and fibroblast cell lines. Utilizing a plaque reduction assay we found that acyclovir potently inhibited the HSV-1 replication in macrophages (EC50 = 0.0025 μ M) compared to Vero (EC50 = 8.5 μ M) and MRC-5 (EC50 = 3.3 μ M) cells. The cytotoxicity of acyclovir was not detected at concns. \leq 20 μ M, thus the selective index in macrophages was $>$ 8000. This marked difference in antiherpetic activity between macrophages and fibroblasts was not observed with Foscarnet and PMEA. We suggest that this potent antiviral effect of acyclovir is mainly due to a proficient phosphorylation of the drug and/or

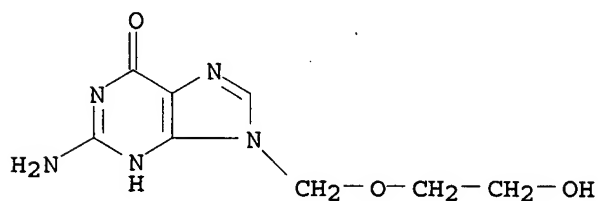
a favorable dGTP/acyclovir triphosphate ratio in macrophage cells.

IT 59277-89-3, Acyclovir 106941-25-7, PMEA
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(potency of acyclovir can be markedly different in different cell types)

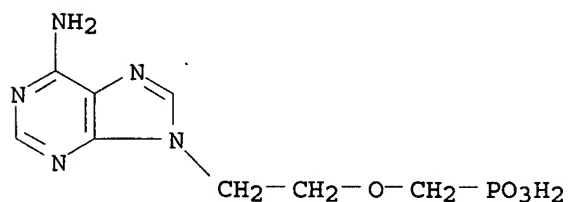
RN 59277-89-3 HCAPLUS

CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[(2-hydroxyethoxy)methyl]- (CA INDEX NAME)



RN 106941-25-7 HCAPLUS

CN Phosphonic acid, P-[[2-(6-amino-9H-purin-9-yl)ethoxy]methyl]- (CA INDEX NAME)



REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 3 OF 38 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2000:446743 HCAPLUS <<LOGINID::20070502>>

DOCUMENT NUMBER: 133:171805

TITLE: Antiviral activities of oral 1-O-hexadecylpropanediol-3-phosphoacyclovir and acyclovir in woodchucks with chronic woodchuck hepatitis virus infection

AUTHOR(S): Hostetler, Karl Y.; Beadle, James R.; Hornbuckle, William E.; Bellezza, Christine A.; Tochkov, Ilia A.; Cote, Paul J.; Gerin, John L.; Korba, Brent E.; Tennant, Bud C.

CORPORATE SOURCE: Department of Medicine, University of California, San Diego, La Jolla, CA, 92093-0676, USA

SOURCE: Antimicrobial Agents and Chemotherapy (2000), 44(7), 1964-1969

CODEN: AMACCQ; ISSN: 0066-4804

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

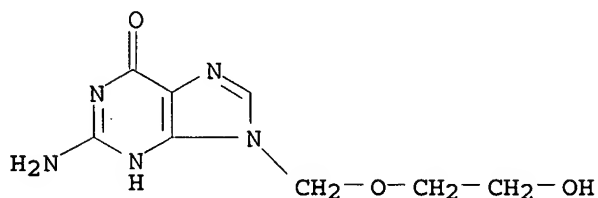
AB Acyclovir triphosphate is a potent inhibitor of hepatitis B virus DNA polymerase, but acyclovir treatment provides no benefit in patients with hepatitis B virus infection. This is due in part to the fact that hepatitis B virus, unlike herpes

simplex virus, does not code for a viral thymidine kinase which catalyzes the initial phosphorylation of acyclovir. We synthesized 1-O-octadecyl-sn-glycero-3-phospho (3-P)-acyclovir and found that it was highly active in reducing hepatitis B virus replication in 2.2.15 cells, while acyclovir was inactive. The greater antiviral activity of 1-O-octadecyl-sn-glycero-3-P-acyclovir appeared to be due to liver cell metabolism of the compound to acyclovir monophosphate.

However, a closely related compound without a hydroxyl group at the sn-2 position of glycerol, 1-O-hexadecylpropanediol-3-P-acyclovir, was more active and selective in 2.2.15 cells in vitro. In this study, we treated woodchucks chronically infected with woodchuck hepatitis virus with increasing oral doses of 1-O-hexadecylpropanediol-3-P-acyclovir and assessed the response to therapy vs. acyclovir or a placebo. At a dosage of 10 mg/kg of body weight twice a day, the test compound significantly inhibited viral replication in vivo, as indicated by a 95% reduction in serum woodchuck hepatitis virus DNA levels and by a 54% reduction in levels of woodchuck hepatitis virus replicative intermediates in the liver. Higher doses were somewhat less effective. In contrast, 20 mg of acyclovir/kg twice daily, a 5.3-fold-higher molar dosage, had no demonstrable activity against woodchuck hepatitis virus. Oral 1-O-hexadecylpropanediol-3-P-acyclovir appeared to be safe and effective in chronic woodchuck hepatitis virus infection.

IT 59277-89-3, Acyclovir
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (antiviral activities of oral 1-O-hexadecylpropanediol-3-phosphoacyclovir and acyclovir in woodchucks with chronic woodchuck hepatitis virus infection)

RN 59277-89-3 HCAPLUS
 CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[(2-hydroxyethoxy)methyl]- (CA INDEX NAME)



REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 4 OF 38 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2000:182395 HCAPLUS <<LOGINID::20070502>>
 DOCUMENT NUMBER: 132:342844
 TITLE: Efficacy of topical acyclovir monophosphate, acyclovir, or penciclovir in orofacial HSV-1 infections of mice and genital HSV-2 infections of guinea pigs
 AUTHOR(S): Kern, Earl R.; Palmer, Joyce; Szczech, George; Painter, George; Hostetler, Karl Y.
 CORPORATE SOURCE: University of Alabama School of Medicine, Birmingham, AL, 35294-2170, USA
 SOURCE: Nucleosides, Nucleotides & Nucleic Acids (2000), 19(1 & 2), 501-513
 CODEN: NNNAFY; ISSN: 1525-7770
 PUBLISHER: Marcel Dekker, Inc.
 DOCUMENT TYPE: Journal

LANGUAGE: English

AB The purpose of these studies was to compare the efficacy of acyclovir monophosphate (ACVMP), acyclovir (ACV), or penciclovir (PCV) against HSV-1 in an orofacial infection of mice and against ACV sensitive and resistant genital HSV-2 infections of guinea pigs. Treatment was initiated 24, 48, or 72 h post inoculation with 5% ACVMP, 5% ACV (Zovirax) or 1% PCV (Denavir). In all expts., similar efficacy was obtained for ACVMP and ACV, whereas PCV was considerably less effective.

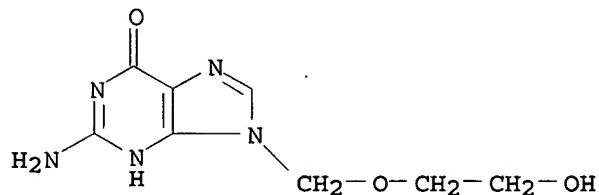
IT 59277-89-3, Zovirax 66341-16-0, Acyclovir monophosphate

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(efficacy of topical acyclovir monophosphate, acyclovir, or penciclovir in orofacial HSV-1 infections of mice and genital HSV-2 infections of guinea pigs)

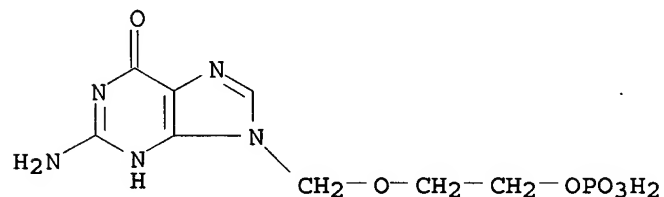
RN 59277-89-3 HCAPLUS

CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[(2-hydroxyethoxy)methyl]- (CA INDEX NAME)



RN 66341-16-0 HCAPLUS

CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[[2-(phosphonoxy)ethoxy]methyl]- (CA INDEX NAME)



REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 5 OF 38 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:310240 HCAPLUS <<LOGINID::20070502>>

DOCUMENT NUMBER: 131:110946

TITLE: Interaction of the recombinant Herpes Simplex Virus type 1 thymidine kinase with thymidine and aciclovir: a kinetic study

AUTHOR(S): Kussmann-Gerber, Susanna; Wurth, Christine; Scapozza, Leonardo; Pilger, Beatrice D.; Pliska, Vladimir; Folkers, Gerd

CORPORATE SOURCE: Department of Pharmacy, Swiss Federal Institute of Technology (ETH), Zurich, CH-8057, Switz.

SOURCE: Nucleosides & Nucleotides (1999), 18(3), 311-330

CODEN: NUNUD5; ISSN: 0732-8311

PUBLISHER: Marcel Dekker, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Herpes Simplex Virus type 1 thymidine kinase (HSV 1 TK) is a key target for antiviral therapy and it phosphorylates a broad spectrum of nucleosides and nucleotides. The authors report the results from kinetic and inhibition expts. with HSV 1 TK, and show that there is a preferred, but not exclusive, binding order of substrates, i.e. dT binds prior to ATP. Furthermore, the results provide new informations on the mechanism of binding suggesting that HSV1 TK undergoes conformational changes during the catalytic cycle.

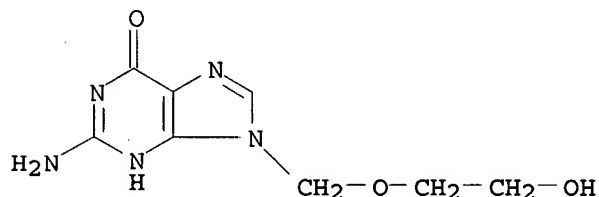
IT 59277-89-3, Aciclovir

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(interaction of recombinant Herpes Simplex Virus type 1 thymidine kinase with thymidine and aciclovir in kinetic study in relation to ATP binding and structure)

RN 59277-89-3 HCAPLUS

CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[(2-hydroxyethoxy)methyl]- (CA INDEX NAME)



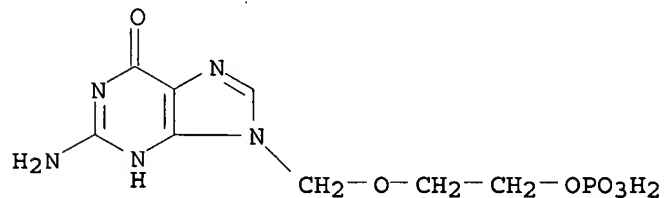
IT 66341-16-0, Acyclovir monophosphate

RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)

(interaction of recombinant Herpes Simplex Virus type 1 thymidine kinase with thymidine and aciclovir in kinetic study in relation to ATP binding and structure)

RN 66341-16-0 HCAPLUS

CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[[2-(phosphonoxy)ethoxy)methyl]- (CA INDEX NAME)



REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 6 OF 38 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:175589 HCAPLUS <<LOGINID::20070502>>

DOCUMENT NUMBER: 130:218263

TITLE: Nucleoside analog phosphates for topical use in the treatment of herpes virus infections

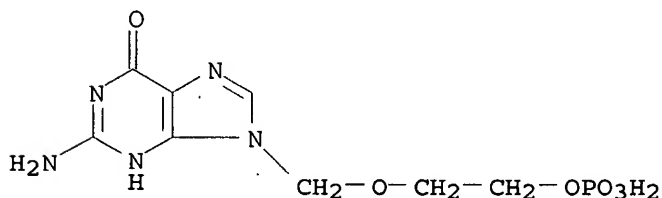
INVENTOR(S): Hostetler, Karl Y.
 PATENT ASSIGNEE(S): USA
 SOURCE: U.S., 19 pp., Cont.-in-part of U.S. 5,580,571.
 CODEN: USXXAM
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 5
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5879700	A	19990309	US 1995-480456	19950607 <--
US 5580571	A	19961203	US 1993-60258	19930512 <--
CA 2222154	A1	19961219	CA 1996-2222154	19960606 <--
WO 9640088	A1	19961219	WO 1996-US10085	19960606 <--
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN				
AU 9663842	A	19961230	AU 1996-63842	19960606 <--
EP 831794	A1	19980401	EP 1996-923289	19960606 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
CN 1192138	A	19980902	CN 1996-195922	19960606 <--
JP 11507642	T	19990706	JP 1997-502194	19960606 <--
CN 1221609	A	19990707	CN 1998-123863	19981030 <--
PRIORITY APPLN. INFO.:				
			US 1991-777683	B2 19911015
			US 1993-60258	A2 19930512
			US 1995-480456	A 19950607
			WO 1996-US10085	W 19960606

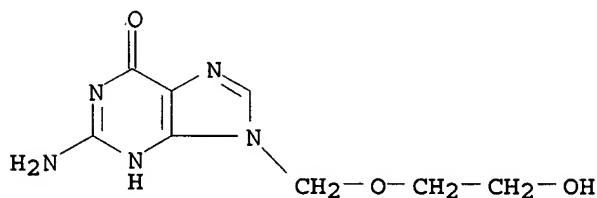
AB Compns. for topical use in herpes virus infections comprise anti-herpes nucleoside analog phosphate esters, e.g. acyclovir monophosphate, acyclovir diphosphate, and acyclovir triphosphate which show increased activity against native strains of herpes virus as well as against resistant strains, particularly thymidine kinase neg. strains of virus. Also disclosed are methods for treatment of herpes infections with nucleoside phosphates. Anti-herpes nucleoside analogs phosphate esters include the phosphoramidates and phosphothiorates, as well as polyphosphates comprising C and S bridging atoms.

IT 66341-16-0P, Acyclovir monophosphate
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (nucleoside analog phosphates for topical use in treatment of herpes virus infections)

RN 66341-16-0 HCAPLUS
 CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[[2-(phosphonooxy)ethoxy]methyl]-
 (CA INDEX NAME)



IT 59277-89-3, Acyclovir
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (reaction; nucleoside analog phosphates for topical use in treatment of
 herpes virus infections)
 RN 59277-89-3 HCAPLUS
 CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[(2-hydroxyethoxy)methyl]- (CA
 INDEX NAME)



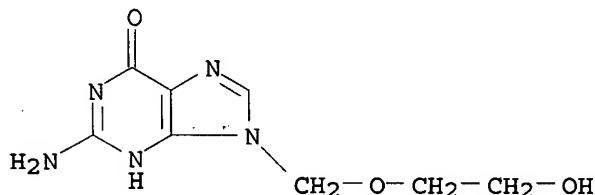
REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 7 OF 38 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1998:588895 HCAPLUS <<LOGINID::20070502>>
 DOCUMENT NUMBER: 129:298069
 TITLE: Superior cytotoxicity with ganciclovir compared with
 acyclovir and 1- β -D-arabinofuranosylthymine in
 herpes simplex virus-thymidine
 kinase-expressing cells: a novel paradigm for cell
 killing
 AUTHOR(S): Rubsam, Laura Z.; Davidson, Beverly L.; Shewach, Donna
 S.
 CORPORATE SOURCE: Department of Pharmacology, University of Michigan
 Medical Center, Ann Arbor, MI, 48109-0504, USA
 SOURCE: Cancer Research (1998), 58(17), 3873-3882
 CODEN: CNREA8; ISSN: 0008-5472
 PUBLISHER: American Association for Cancer Research
 DOCUMENT TYPE: Journal
 LANGUAGE: English

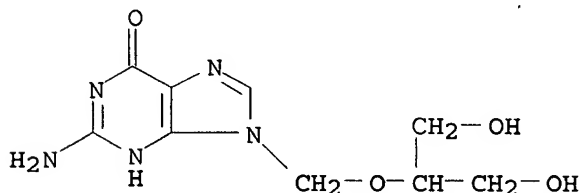
AB Enzyme-prodrug therapy using ganciclovir and herpes simplex
 virus-thymidine kinase (HSV-TK) has demonstrated excellent antitumor
 activity in many different types of malignant cells. Previously, the
 authors noted that ganciclovir was substantially more cytotoxic than other
 HSV-TK substrates. Therefore, the authors embarked on a study to determine the
 basis for the superior cytotoxicity of ganciclovir. In U251tk human
 glioblastoma cells that stably express HSV-TK, ganciclovir elicited a >4
 log cell kill instead of the ≤ 1.5 log cell kill mediated by two
 other HSV-TK substrates, 1- β -D-arabinofuranosylthymine (araT) and
 acyclovir. Study of the metabolism of these drugs demonstrated that acyclovir
 was poorly phosphorylated to its active triphosphate with DNA
 incorporation below the limit of detection, which may explain the <1 log
 cell kill in these cells. Lower levels of ganciclovir triphosphate
 accumulated compared with araT triphosphate (araTTP) under conditions that
 induced ≥ 1 log cell kill (67 vs. 1235 pmol/107 cells, resp.), and
 the half-life for the triphosphate of ganciclovir was shorter than that of
 araT (terminal half-lives of 15 and 41 h, resp.). Incorporation of
 ganciclovir monophosphate into DNA was less than that of araT
 monophosphate, and both analogs were retained in DNA for ≥ 48 h.
 Thus, the superior cytotoxicity of ganciclovir was not due to enhanced
 metabolism to active forms. Highly cytotoxic concns. of ganciclovir produced
 only weak inhibition of DNA synthesis. This allowed cells to proceed
 through S and G2-M phases during and after drug exposure, resulting in a

doubling of cell number by 48 h after drug washout. As they attempted to progress through the cell cycle a second time, ganciclovir-treated cells accumulated in early S-phase and remained there until cell death, suggesting that ganciclovir incorporation in the DNA template was important for cytotoxicity. In contrast, strong inhibition of DNA synthesis by araTTP prevented cells from traversing the cell cycle for at least 12 h after drug washout, when the active metabolite was largely degraded. AraT-treated cells were unable to divide for at least 72 h after drug exposure, at which point the surviving cells displayed a normal cell cycle distribution pattern. Based on the results presented here, the authors propose a novel paradigm in which the ability of ganciclovir to incorporate into DNA without inhibiting progression through S-phase, combined with high cytotoxicity for incorporated ganciclovir monophosphate, produces multilog cytotoxicity.

IT 59277-89-3, Acyclovir 82410-32-0, Ganciclovir
 RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
 (superior cytotoxicity with ganciclovir compared with acyclovir and D-arabinofuranosylthymine in herpes simplex virus-thymidine kinase-expressing cells in relation to metabolism and incorporation into DNA and apoptosis)
 RN 59277-89-3 HCAPLUS
 CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[(2-hydroxyethoxy)methyl]- (CA INDEX NAME)

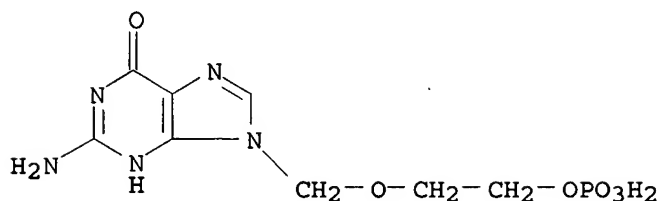


RN 82410-32-0 HCAPLUS
 CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[[2-hydroxy-1-(hydroxymethyl)ethoxy]methyl]- (CA INDEX NAME)



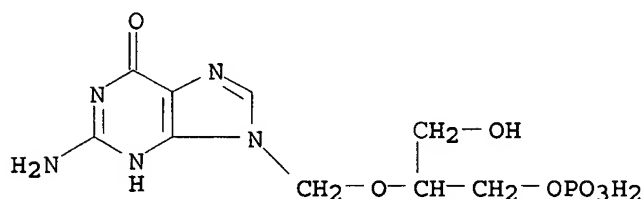
IT 66341-16-0, Acyclovir monophosphate
 86761-39-9
 RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
 (superior cytotoxicity with ganciclovir compared with acyclovir and D-arabinofuranosylthymine in herpes simplex virus-thymidine kinase-expressing cells in relation to metabolism and incorporation into DNA and apoptosis)
 RN 66341-16-0 HCAPLUS
 CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[[2-(phosphonoxy)ethoxy]methyl]-

(CA INDEX NAME)



RN 86761-39-9 HCAPLUS

CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[[1-(hydroxymethyl)-2-(phosphonoxy)ethoxy]methyl]- (CA INDEX NAME)



REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 8 OF 38 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1998:516837 HCAPLUS <<LOGINID::20070502>>

DOCUMENT NUMBER: 129:239501

TITLE: Mode of action of (1'S,2'R)-9-[[1',2'-bis(hydroxymethyl)cycloprop-1'-yl]methyl]guanine (A-5021) against herpes simplex virus Type 1 and Type 2 and varicella-zoster virus

AUTHOR(S): Ono, Nobukazu; Iwayama, Satoshi; Suzuki, Katsuya; Sekiyama, Takaaki; Nakazawa, Harumi; Tsuji, Takashi; Okunishi, Masahiko; Daikoku, Tohru; Nishiyama, Yukihiko

CORPORATE SOURCE: Life Science Laboratories, Ajinomoto Co., Inc., Yokohama, 244, Japan

SOURCE: Antimicrobial Agents and Chemotherapy (1998), 42(8), 2095-2102
CODEN: AMACQ; ISSN: 0066-4804

PUBLISHER: American Society for Microbiology

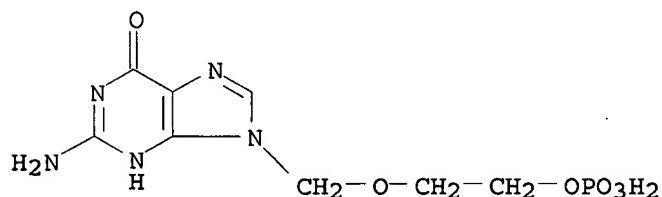
DOCUMENT TYPE: Journal

LANGUAGE: English

AB The mode of action of (1'S,2'R)-9-[[1',2'-bis(hydroxymethyl)cycloprop-1'-yl]methyl]guanine (A-5021) against herpes simplex virus type 1 (HSV-1), HSV-2, and varicella-zoster virus (VZV) was studied. A-5021 was monophosphorylated at the 2' site by viral thymidine kinases (TKs). The 50% inhibitory values for thymidine phosphorylation of A-5021 by HSV-1 TK and HSV-2 TK were comparable to those for penciclovir (PCV) and lower than those for acyclovir (ACV). Of these three agents, A-5021 inhibited VZV TK most efficiently. A-5021 was phosphorylated to a mono-, di-, and triphosphate in MRC-5 cells infected with HSV-1, HSV-2, and VZV. A-5021 triphosphate accumulated more than ACV triphosphate but less than PCV triphosphate in MRC-5 cells infected with HSV-1 or VZV, whereas HSV-2-infected MRC-5 cells had comparable levels of A-5021 and ACV triphosphates. The intracellular half-life of A-5021 triphosphate was

considerably longer than that of ACV triphosphate and shorter than that of PCV triphosphate. A-5021 triphosphate competitively inhibited HSV DNA polymerases with respect to dGTP. Inhibition was strongest with ACV triphosphate, followed by A-5021 triphosphate and then (R,S)-PCV triphosphate. A DNA chain elongation experiment revealed that A-5021 triphosphate was incorporated into DNA instead of dGTP and terminated elongation, although limited chain extension was observed. Thus, the strong antiviral activity of A-5021 appears to depend on a more rapid and stable accumulation of its triphosphate in infected cells than that of ACV and on stronger inhibition of viral DNA polymerase by its triphosphate than that of PCV.

IT 66341-16-0P, Acyclovir monophosphate
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 ((1'S,2'R)-9-{[1',2'-bis(hydroxymethyl)cycloprop-1'-yl]methyl}guanine (A-5021) action against herpes simplex virus Type 1 and Type 2 and varicella-zoster virus)
 RN 66341-16-0 HCAPLUS
 CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[[2-(phosphonoxy)ethoxy]methyl]- (CA INDEX NAME)



REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 9 OF 38 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1997:804941 HCAPLUS <<LOGINID::20070502>>

DOCUMENT NUMBER: 128:123480

TITLE: Synthesis, biological activity and decomposition studies of amino acid phosphomonoester amidates of acyclovir

AUTHOR(S): Abraham, Timothy W.; McIntee, Edward J.; Iyer, Vidhya V.; Schinazi, Raymond F.; Wagner, Carston R.

CORPORATE SOURCE: Department of Medicinal Chemistry, College of Pharmacy, University of Minnesota, Minneapolis, MN, 55455, USA

SOURCE: Nucleosides & Nucleotides (1997), 16(10 & 11), 2079-2092

CODEN: NUNUD5; ISSN: 0732-8311

PUBLISHER: Marcel Dekker, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

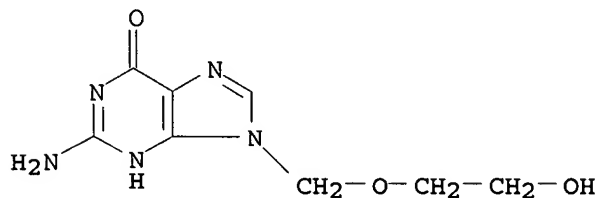
AB Highly stable and water soluble amino acid phosphomonoester amidates of acyclovir (ACV) were synthesized and shown to function predominantly as prodrugs of ACV and not acyclovir monophosphate (ACV-MP) with activities within two fold of the amino acid prodrug of ACV, valaciclovir (VACV). Metabolism studies revealed that incubation of cell-free exts. of Vero cells with the L-leucine phosphomonoester amide of ACV (3c), resulted in a burst of ACV-MP production followed by the rapid generation of ACV.

IT 59277-89-3, Acyclovir
 RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation and anti-HSV activity of amino acid phosphomonoester amidates of acyclovir)

RN 59277-89-3 HCAPLUS

CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[(2-hydroxyethoxy)methyl]- (CA INDEX NAME)



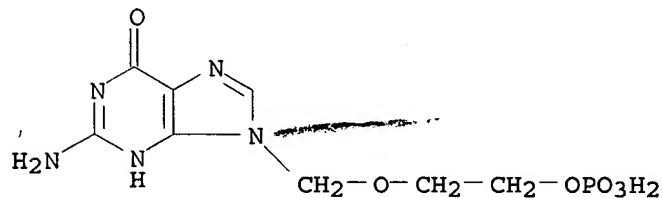
IT 66341-16-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and anti-HSV activity of amino acid phosphomonoester amidates of acyclovir)

RN 66341-16-0 HCAPLUS

CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[[2-(phosphonoxy)ethoxy]methyl]- (CA INDEX NAME)



REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 10 OF 38 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1997:121416 HCAPLUS <<LOGINID::20070502>>

DOCUMENT NUMBER: 126:135594

TITLE: Acyclovir derivatives for topical use

INVENTOR(S): Hostetler, Karl Y.

PATENT ASSIGNEE(S): Hostetler, Karl Y., USA

SOURCE: PCT Int. Appl., 34 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 5

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9640088	A1	19961219	WO 1996-US10085	19960606 <--
W:	AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG			
RW:	KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN			
US 5879700	A	19990309	US 1995-480456	19950607 <--

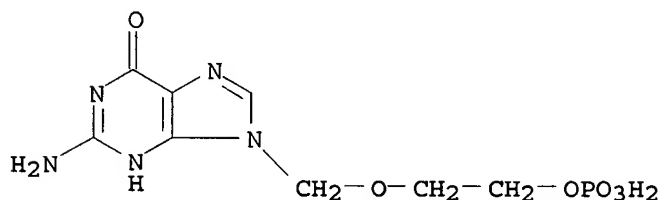
AU 9663842	A	19961230	AU 1996-63842	19960606	<--
EP 831794	A1	19980401	EP 1996-923289	19960606	<--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
JP 11507642	T	19990706	JP 1997-502194	19960606	<--
PRIORITY APPLN. INFO.:			US 1995-480456	A	19950607
			US 1991-777683	B2	19911015
			US 1993-60258	A2	19930512
			WO 1996-US10085	W	19960606

AB The invention involves compns. for topical use in herpes virus infections comprising anti-herpes nucleoside analog phosphate esters, such as acyclovir monophosphate, acyclovir diphosphate, and acyclovir triphosphate, which show increased activity against native strains of herpes virus as well as against resistant strains, particularly thymidine kinase neg. strains of virus. Anti-herpes nucleoside analogs phosphate esters include the phosphoramidates and phosphothiorates, as well as polyphosphates comprising C and S bridging atoms.

IT 66341-16-0, Acyclovir monophosphate
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); PROC (Process); RACT (Reactant or reagent); USES (Uses)
(acyclovir derivs. for topical use against herpes virus infections)

RN 66341-16-0 HCAPLUS

CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[[2-(phosphonoxy)ethoxy]methyl]-
(CA INDEX NAME)

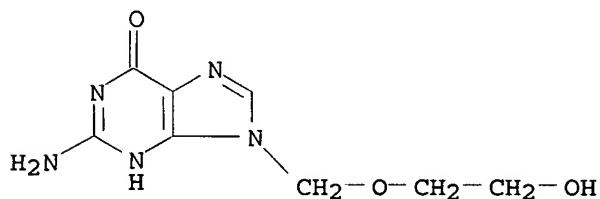


IT 59277-89-3, Acyclovir

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(acyclovir derivs. for topical use against herpes virus infections)

RN 59277-89-3 HCAPLUS

CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[(2-hydroxyethoxy)methyl]- (CA
INDEX NAME)

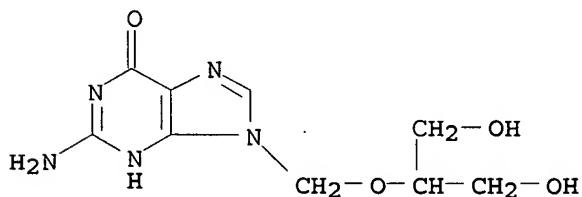


IT 82410-32-0

RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(acyclovir derivs. for topical use against herpes virus infections)

RN 82410-32-0 HCAPLUS

CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[[2-hydroxy-1-(hydroxymethyl)ethoxy]methyl]- (CA INDEX NAME)



=> s thymidine kinase

54446 THYMIDINE

328 THYMIDINES

54565 THYMIDINE

(THYMIDINE OR THYMIDINES)

289463 KINASE

55888 KINASES

298557 KINASE

(KINASE OR KINASES)

L11 9845 THYMIDINE KINASE

(THYMIDINE (W) KINASE)

=> d his

(FILE 'HOME' ENTERED AT 15:58:27 ON 02 MAY 2007)

FILE 'HCAPLUS' ENTERED AT 15:58:36 ON 02 MAY 2007

E US20040259832/PN 25

L1 1 S E3

FILE 'STNGUIDE' ENTERED AT 15:59:26 ON 02 MAY 2007

FILE 'HCAPLUS' ENTERED AT 16:02:09 ON 02 MAY 2007

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L3 237600 S (9002-89-5 OR 9004-34-6 OR 9005-25-8 OR 9012-36-6 OR 24980-4

L4 276194 S L2 OR L3

L5 1 S L4 AND L1

FILE 'STNGUIDE' ENTERED AT 16:03:41 ON 02 MAY 2007

FILE 'HCAPLUS' ENTERED AT 16:07:58 ON 02 MAY 2007

L6 6746 S (59277-89-3 OR 66341-16-0 OR 82410-32-0 OR 86761-39-9 OR 104
E HERPES+ALL/CT

L7 2471 S L6 AND (HERPES OR "HERPES" OR "INFECTION" (L) "HERPES" OR "SK

L8 113 S ACYCLOVIR ?PHOSPHATE?

L9 40 S L8 AND L7

L10 38 S L9 AND 1800<=PY<=2003

L11 9845 S THYMIDINE KINASE

=> s l11 and l10

L12 24 L11 AND L10

=> s thymidine kinase inhibitor

54446 THYMIDINE

328 THYMIDINES

54565 THYMIDINE

(THYMIDINE OR THYMIDINES)

289463 KINASE

55888 KINASES

298557 KINASE

(KINASE OR KINASES)

538149 INHIBITOR

542706 INHIBITORS

846539 INHIBITOR

(INHIBITOR OR INHIBITORS)

L13 76 THYMIDINE KINASE INHIBITOR

(THYMIDINE (W) KINASE (W) INHIBITOR)

=> s l13 and l12

L14 0 L13 AND L12

=> d l12 ti 1-24

L12 ANSWER 1 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN

TI Antiviral activity of cyclosaligenyl prodrugs of acyclovir, carbovir, and abacavir

L12 ANSWER 2 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN

TI Antiviral activities of oral 1-O-hexadecylpropanediol-3-phosphoacyclovir and acyclovir in woodchucks with chronic woodchuck hepatitis virus infection

L12 ANSWER 3 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN

TI Interaction of the recombinant Herpes Simplex Virus type 1 thymidine kinase with thymidine and aciclovir: a kinetic study

L12 ANSWER 4 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN

TI Nucleoside analog phosphates for topical use in the treatment of herpes virus infections

L12 ANSWER 5 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN

TI Superior cytotoxicity with ganciclovir compared with acyclovir and 1-β-D-arabinofuranosylthymine in herpes simplex virus-thymidine kinase-expressing cells: a novel paradigm for cell killing

L12 ANSWER 6 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN

TI Mode of action of (1'S,2'R)-9-{[1',2'-bis(hydroxymethyl)cycloprop-1'-yl]methyl}guanine (A-5021) against herpes simplex virus Type 1 and Type 2 and varicella-zoster virus

L12 ANSWER 7 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN

TI Acyclovir derivatives for topical use

L12 ANSWER 8 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN

TI Historical aspects of anti-herpesvirus research leading to the discovery of acyclovir

L12 ANSWER 9 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN

TI Nucleoside analogs for topical use in herpesvirus infections

L12 ANSWER 10 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN

TI Herpes simplex virus resistance to acyclovir: Clinical relevance

- L12 ANSWER 11 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN
TI A comparative study of the in vitro and in vivo antiviral activities of acyclovir and penciclovir
- L12 ANSWER 12 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Acyclovir derivatives and other nucleoside analogs for topical treatment of herpes infection
- L12 ANSWER 13 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Acyclovir diphosphate dimyristoylglycerol: a phospholipid prodrug with activity against acyclovir-resistant herpes simplex virus
- L12 ANSWER 14 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Inhibition of herpes simplex virus type 1 DNA polymerase by [1R(1 α ,2 β ,3 α)]-9-[2,3-bis(hydroxymethyl)cyclobutyl]guanin
e
- L12 ANSWER 15 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Herpes simplex virus type 1 DNA polymerase. Mechanism of inhibition by acyclovir triphosphate
- L12 ANSWER 16 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Effects of various nucleosides on antiviral activity and metabolism of 1- β -D-arabinofuranosyl-E-5-(2-bromovinyl)uracil against herpes simplex virus types 1 and 2
- L12 ANSWER 17 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Antiviral activities of guanosine analogs in guinea pig embryonic fibroblasts
- L12 ANSWER 18 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Solution conformations of some acyclonucleoside and nucleotide analogs of antiviral acyclonucleosides, and their substrate/inhibitor properties in several enzyme systems
- L12 ANSWER 19 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Cooperative effects between two acyclovir resistance loci in herpes simplex virus
- L12 ANSWER 20 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Selectivity of antiviral effectiveness derived from differences of herpes simplex virus-coded thymidine kinases
- L12 ANSWER 21 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN
TI A perspective on resistance to acyclovir in herpes simplex virus
- L12 ANSWER 22 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Acyclovir-resistant mutants of herpes simplex virus type 1 express altered DNA polymerase or reduced acyclovir phosphorylating activities
- L12 ANSWER 23 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Laboratory studies on acyclovir
- L12 ANSWER 24 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN
TI The chemotherapeutic exploitation of virus-specified enzymes

=> s cidofovir

L15 684 CIDOFOVIR

=> s l15 and l17

L16 89 L15 AND L7

=> s l16 and l10

L17 0 L16 AND L10

=> s ganciclovir monophosphate

5 GANCILOVIR
31705 MONOPHOSPHATE
4114 MONOPHOSPHATES
34622 MONOPHOSPHATE
(MONOPHOSPHATE OR MONOPHOSPHATES)

L18 0 GANCILOVIR MONOPHOSPHATE
(GANCILOVIR (W) MONOPHOSPHATE)

=> s ganciclovir

L19 3504 GANCICLOVIR

=> s ganciclovir monophosphate

3504 GANCICLOVIR
31705 MONOPHOSPHATE
4114 MONOPHOSPHATES
34622 MONOPHOSPHATE
(MONOPHOSPHATE OR MONOPHOSPHATES)

L20 11 GANCICLOVIR MONOPHOSPHATE
(GANCICLOVIR (W) MONOPHOSPHATE)

=> s l20 and l7

L21 2 L20 AND L7

=> d l21 ibib abs hitstr

L21 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1998:588895 HCAPLUS <<LOGINID::20070502>>

DOCUMENT NUMBER: 129:298069

TITLE: Superior cytotoxicity with ganciclovir compared with acyclovir and 1- β -D-arabinofuranosylthymine in herpes simplex virus-thymidine kinase-expressing cells: a novel paradigm for cell killing

AUTHOR(S): Rubsam, Laura Z.; Davidson, Beverly L.; Shewach, Donna S.

CORPORATE SOURCE: Department of Pharmacology, University of Michigan Medical Center, Ann Arbor, MI, 48109-0504, USA

SOURCE: Cancer Research (1998), 58(17), 3873-3882

CODEN: CNREA8; ISSN: 0008-5472

PUBLISHER: American Association for Cancer Research

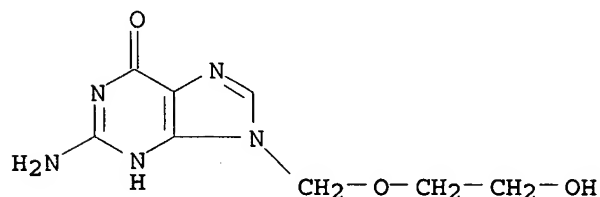
DOCUMENT TYPE: Journal

LANGUAGE: English

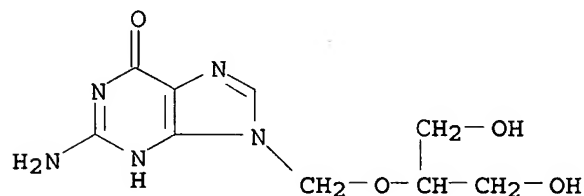
AB Enzyme-prodrug therapy using ganciclovir and herpes simplex virus-thymidine kinase (HSV-TK) has demonstrated excellent antitumor activity in many different types of malignant cells. Previously, the authors noted that ganciclovir was substantially more cytotoxic than other HSV-TK substrates. Therefore, the authors embarked on a study to determine the basis for the superior cytotoxicity of ganciclovir. In U251tk human glioblastoma cells that stably express HSV-TK, ganciclovir elicited a >4 log cell kill instead of the ≤ 1.5 log cell kill mediated by two other HSV-TK substrates, 1- β -D-arabinofuranosylthymine (araT) and acyclovir. Study of the metabolism of these drugs demonstrated that acyclovir was poorly phosphorylated to its active triphosphate with DNA incorporation below the limit of detection, which may explain the <1 log cell kill in these cells. Lower levels of ganciclovir triphosphate accumulated compared with araT triphosphate (araTTP) under conditions that induced ≥ 1 log cell kill (67 vs. 1235 pmol/107 cells, resp.), and

the half-life for the triphosphate of ganciclovir was shorter than that of araT (terminal half-lives of 15 and 41 h, resp.). Incorporation of ganciclovir monophosphate into DNA was less than that of araT monophosphate, and both analogs were retained in DNA for ≥ 48 h. Thus, the superior cytotoxicity of ganciclovir was not due to enhanced metabolism to active forms. Highly cytotoxic concns. of ganciclovir produced only weak inhibition of DNA synthesis. This allowed cells to proceed through S and G2-M phases during and after drug exposure, resulting in a doubling of cell number by 48 h after drug washout. As they attempted to progress through the cell cycle a second time, ganciclovir-treated cells accumulated in early S-phase and remained there until cell death, suggesting that ganciclovir incorporation in the DNA template was important for cytotoxicity. In contrast, strong inhibition of DNA synthesis by araTTP prevented cells from traversing the cell cycle for at least 12 h after drug washout, when the active metabolite was largely degraded. AraT-treated cells were unable to divide for at least 72 h after drug exposure, at which point the surviving cells displayed a normal cell cycle distribution pattern. Based on the results presented here, the authors propose a novel paradigm in which the ability of ganciclovir to incorporate into DNA without inhibiting progression through S-phase, combined with high cytotoxicity for incorporated ganciclovir monophosphate, produces multilog cytotoxicity.

IT 59277-89-3, Acyclovir 82410-32-0, Ganciclovir
 RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
 (superior cytotoxicity with ganciclovir compared with acyclovir and D-arabinofuranosylthymine in herpes simplex virus-thymidine kinase-expressing cells in relation to metabolism and incorporation into DNA and apoptosis)
 RN 59277-89-3 HCAPLUS
 CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[(2-hydroxyethoxy)methyl]- (CA INDEX NAME)



RN 82410-32-0 HCAPLUS
 CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[[2-hydroxy-1-(hydroxymethyl)ethoxy]methyl]- (CA INDEX NAME)



IT 66341-16-0, Acyclovir monophosphate 86761-39-9
 RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation,

substance identification.

=> s forscarnet

L22 3 FORSCARNET

=> s foscarnet

L23 857 FOSCARNET

=> s l23 and l7

L24 121 L23 AND L7

=> S L24 AND 1800<=PY<=2003

23932189 1800<=PY<=2003

L25 93 L24 AND 1800<=PY<=2003

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MISSING OPERATOR L25 IBIB

The search profile that was entered contains terms or nested terms that are not separated by a logical operator.

=> d l25 ibib abs hitstr 1-5

L25 ANSWER 1 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:741595 HCAPLUS <<LOGINID::20070502>>

DOCUMENT NUMBER: 140:104511

TITLE: Comparison of HSV-1 thymidine kinase-dependent and -independent inhibition of replication-competent adenoviral vectors by a panel of drugs

AUTHOR(S): Wildner, Oliver; Hoffmann, Dennis; Jogler, Christian; Ueberla, Klaus

CORPORATE SOURCE: Bldg. MA, Abteilung fuer Molekulare und Medizinische Virologie, Ruhr-Universitaet Bochum, Bochum, D-44801, Germany

SOURCE: Cancer Gene Therapy (2003), 10(10), 791-802

CODEN: CGTHEG; ISSN: 0929-1903

PUBLISHER: Nature Publishing Group

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Replication-competent adenoviral vectors hold the promise to be more efficient gene delivery vehicles than their replication-deficient counterparts, but they are also associated with a higher risk for adverse effects, especially in light of the fact that there is no established effective therapy for serious, disseminated adenovirus infection. To assess whether the therapeutic options to inhibit adenoviral replication can be enhanced by expressing a suicide gene, we examined the antiadenoviral effects of 15 drugs against wild-type adenovirus type 5 (Ad5) and an Ad5-based replication-competent vector expressing herpes simplex virus-1 thymidine kinase (HSV-tk) (Ad.OW34) using a real-time polymerase chain reaction -based assay and flow cytometry. Ad5 and Ad.OW34 were highly susceptible to the fluorinated pyrimidine analogs 5-fluoro-2'-deoxyuridine (FUDR), 5-fluorouridine (FUR), and trifluorothymidine (TFT), with a mean 50% inhibitory concentration (IC50) ranging from 0.12 to 0.32 μ M. The mean IC50 of ribavirin and cidofovir (CDV) for Ad5, the most frequently used drugs to treat adenovirus disease, was 6.87 and 3.19 μ M, resp. In contrast to Ad5, the Ad.OW34 vector was susceptible to (E)-5-(2-bromovinyl)-2'-deoxyuridine (BVdU, IC50 0.09 μ M), ganciclovir (GCV, IC50 0.19 μ M), and acyclovir (ACV, IC50 32.04 μ M). Addnl., we demonstrated in an animal model that Ad.OW34 vector replication can be inhibited significantly by GCV, CDV, and TFT by 35.2, 7.7, and 3.7-fold, resp., compared to untreated animals. The observed antiadenoviral effects were primarily not through cell killing, since the in vitro 50% cytotoxic concns. (CC50) were more than 1000 times higher than the antiadenoviral IC50 of the drugs examined, even in cells stably

expressing HSV-tk. Since for HSV-tk-dependent inhibition of adenoviral vectors, stability of HSV-tk expression is crucial, we examined Ad.OW34 vector stability, by passaging the vector 10 times serially in the presence of 10 μ M GCV. The HSV-tk/GCV system neither changed the susceptibility of Ad.OW34 to GCV significantly nor detectable vector rearrangements occurred, suggesting that the system might be suitable as a fail-safe mechanism to stop adenoviral vector replication.

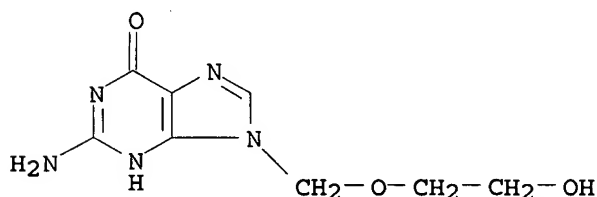
IT 59277-89-3, Acyclovir 82410-32-0, Ganciclovir
113852-37-2, Cidofovir

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)

(inhibition of replication competent adenoviral vectors by a panel of drugs)

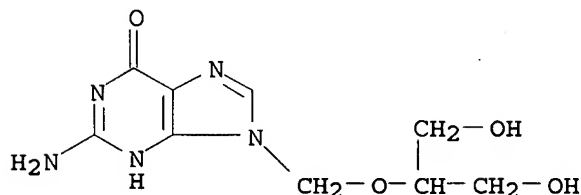
RN 59277-89-3 HCAPLUS

CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[(2-hydroxyethoxy)methyl]- (CA INDEX NAME)



RN 82410-32-0 HCAPLUS

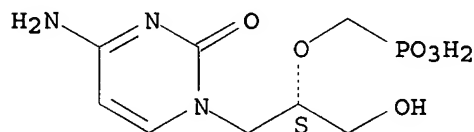
CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[[2-hydroxy-1-(hydroxymethyl)ethoxy]methyl]- (CA INDEX NAME)



RN 113852-37-2 HCAPLUS

CN Phosphonic acid, P-[[[(1S)-2-(4-amino-2-oxo-1(2H)-pyrimidinyl)-1-(hydroxymethyl)ethoxy]methyl]- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 101 THERE ARE 101 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 2 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN

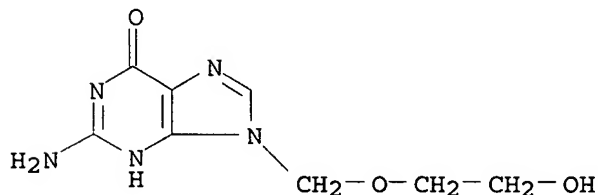
ACCESSION NUMBER: 2003:543502 HCAPLUS <<LOGINID::20070502>>

DOCUMENT NUMBER: 139:357783
 TITLE: Current and potential therapies for the treatment of herpesvirus infections
 AUTHOR(S): Villarreal, Elcira C.
 CORPORATE SOURCE: Lilly Centre for Women's Health, Eli Lilly and Company, Indianapolis, IN, 46285, USA
 SOURCE: Progress in Drug Research (2003), 60, 263-307
 CODEN: FAZMAE; ISSN: 0071-786X
 PUBLISHER: Birkhaeuser Verlag
 DOCUMENT TYPE: Journal; General Review
 LANGUAGE: English

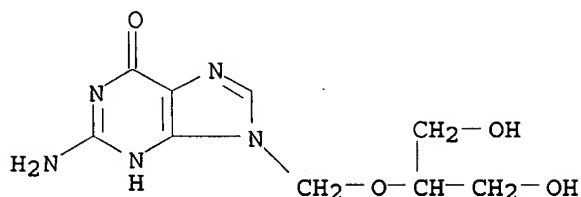
AB A review. Human herpesviruses are found worldwide and are among the most frequent causes of viral infections in immunocompetent as well as in immunocompromised patients. During the past decade and a half a better understanding of the replication and disease-causing state of herpes simplex virus types 1 and 2 (HSV-1 and HSV-2), varicella zoster virus (VZV), and human cytomegalovirus (HCMV) has been achieved due in part to the development of potent antiviral compds. that target these viruses. While some of these antiviral therapies are considered safe and efficacious (acyclovir, penciclovir), some have toxicities associated with them (ganciclovir and foscarnet). In addition, the increased and prolonged use of these compds. in the clin. setting, especially for the treatment of immunocompromised patients, has led to the emergence of viral resistance against most of these drugs. While resistance is not a serious issue for immunocompetent individuals, it is a real concern for immunocompromised patients, especially those with AIDS and the ones that have undergone organ transplantation. All the currently approved treatments target the viral DNA polymerase. It is clear that new drugs that are more efficacious than the present ones, are not toxic, and target a different viral function would be of great use especially for immunocompromised patients. Here, an overview is provided of the diseases caused by the herpesviruses as well as the replication strategy of the better studied members of this family for which treatments are available. We also discuss the various drugs that have been approved for the treatment of some herpesviruses in terms of structure, mechanism of action, and development of resistance. Finally, we present a discussion of viral targets other than the DNA polymerase, for which new antiviral compds. are being considered.

IT 59277-89-3, Acyclovir 82410-32-0, Ganciclovir
 RL: ADV (Adverse effect, including toxicity); DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (current and potential therapies for treatment of herpesvirus infections)

RN 59277-89-3 HCAPLUS
 CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[(2-hydroxyethoxy)methyl]- (CA INDEX NAME)



RN 82410-32-0 HCAPLUS
 CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[[2-hydroxy-1-(hydroxymethyl)ethoxy]methyl]- (CA INDEX NAME)



REFERENCE COUNT: 249 THERE ARE 249 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 3 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2003:526763 HCAPLUS <<LOGINID::20070502>>
 DOCUMENT NUMBER: 139:175724
 TITLE: Drug resistance patterns of recombinant herpes simplex virus DNA polymerase mutants generated with a set of overlapping cosmids and plasmids
 AUTHOR(S): Bestman-Smith, Julie; Boivin, Guy
 CORPORATE SOURCE: Centre de Recherche en Infectiologie of the Centre Hospitalier Universitaire de Quebec (Pavillon CHUL) and Universite Laval, Quebec, Can.
 SOURCE: Journal of Virology (2003), 77(14), 7820-7829
 CODEN: JOVIAM; ISSN: 0022-538X
 PUBLISHER: American Society for Microbiology
 DOCUMENT TYPE: Journal
 LANGUAGE: English

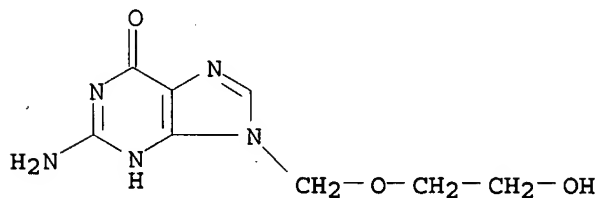
AB Herpes simplex virus (HSV) DNA polymerase (Pol) mutations can confer resistance to all currently available antiherpetic drugs. However, discrimination between mutations responsible for drug resistance and those that are part of viral polymorphism can be difficult with current methodologies. A new system is reported for rapid generation of recombinant HSV type 1 (HSV-1) DNA Pol mutants based on transfection of a set of overlapping viral cosmids and plasmids. With this approach, twenty HSV-1 recombinants with single or dual mutations within the DNA pol gene were successfully generated and subsequently evaluated for their susceptibilities to acyclovir (ACV), foscarnet (FOS), cidofovir (CDV), and adefovir (ADV). Mutations within DNA Pol conserved regions II (A719T and S724N), VI (L778M, D780N, and L782I), and I (F891C) were shown to induce cross-resistance to ACV, FOS, and ADV, with two of these mutations (S724N and L778M) also conferring significant reduction in CDV susceptibility. Mutant F891C was associated with the highest levels of resistance towards ACV and FOS and was strongly impaired in its replication capacity. One mutation (D907V) lying outside of the conserved regions was also associated with this ACV-, FOS-, and ADV-resistant phenotype. Some mutations (K522E and Y577H) within the δ -region C were lethal, whereas others (P561S and V573M) induced no resistance to any of the drugs tested. Recombinants harboring mutations within conserved regions V (N961K) and VII (Y941H) were resistant to ACV but susceptible to FOS. Finally, mutations within conserved region III were associated with various susceptibility profiles. This new system allows a rapid and accurate evaluation of the functional role of various DNA Pol mutations, which should translate into improved management of drug-resistant HSV infections.

IT 59277-89-3, Acyclovir 106941-25-7, Adefovir 113852-37-2, Cidofovir
 RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
 (drug resistance patterns of recombinant herpes simplex virus

DNA polymerase mutants generated with a set of overlapping cosmids and plasmids)

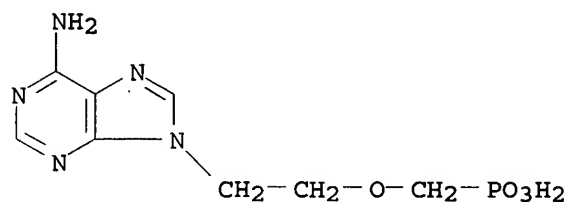
RN 59277-89-3 HCAPLUS

CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[(2-hydroxyethoxy)methyl]- (CA INDEX NAME)



RN 106941-25-7 HCAPLUS

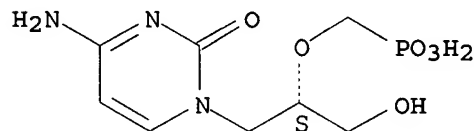
CN Phosphonic acid, P-[[2-(6-amino-9H-purin-9-yl)ethoxy]methyl]- (CA INDEX NAME)



RN 113852-37-2 HCAPLUS

CN Phosphonic acid, P-[(1S)-2-(4-amino-2-oxo-1(2H)-pyrimidinyl)-1-(hydroxymethyl)ethoxy]methyl]- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 4 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:513247 HCAPLUS <<LOGINID::20070502>>

DOCUMENT NUMBER: 139:358071

TITLE: In vitro activities of benzimidazole D- and L-ribonucleosides against herpesviruses

AUTHOR(S): Williams, Stephanie L.; Hartline, Carroll B.; Kushner, Nicole L.; Harden, Emma A.; Bidanset, Deborah J.; Drach, John C.; Townsend, Leroy B.; Underwood, Mark R.; Biron, Karen K.; Kern, Earl R.

CORPORATE SOURCE: University of Alabama School of Medicine, Birmingham, AL, USA

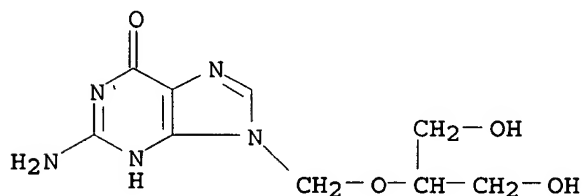
SOURCE: Antimicrobial Agents and Chemotherapy (2003), 47(7), 2186-2192

CODEN: AMACCQ; ISSN: 0066-4804

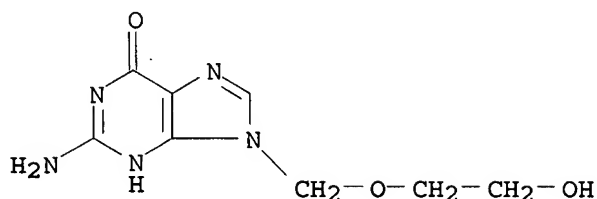
PUBLISHER: American Society for Microbiology
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB Herpes simplex virus types 1 and 2 (HSV-1 and HSV-2), varicella-zoster virus (VZV), cytomegalovirus (CMV), Epstein-Barr virus (EBV), human herpesvirus 6 (HHV-6), and human herpesvirus 8 (HHV-8) are responsible for a number of clin. manifestations in both normal and immunocompromised individuals. The parent benzimidazole ribonucleosides evaluated in this series, 2-bromo-5,6-dichloro-1-(β -D-ribofuranosyl)benzimidazole (BDCRB) and maribavir (1263W94), are potent and selective inhibitors of human CMV replication. These nucleosides act by two different mechanisms. BDCRB blocks the processing and maturation of viral DNA, whereas 1263W94 inhibits the viral enzyme pUL97 and interferes with DNA synthesis. In the present study, we have evaluated the in vitro antiviral activity of BDCRB, an analog, GW275175X (175X), and 1263W94 against the replication of HSV-1, HSV-2, VZV, CMV, EBV, HHV-6, and HHV-8. By using various methodologies, significant activity was observed against human CMV and EBV but not against HSV-1, HSV-2, VZV, HHV-6, or HHV-8. Plaque reduction assays performed on a variety of laboratory and clin. isolates of human CMV indicated that all strains, including those resistant to ganciclovir (GCV) and foscarnet, were sensitive to all three benzimidazole ribonucleosides, with mean 50% effective concentration values of about 1 to 5 μ M compared to that of GCV at 6 μ M. The toxicity of these compds. in tissue culture cells appeared to be similar to that observed with GCV. These results demonstrate that the benzimidazole ribonucleosides are active against human CMV and EBV and suggest that they may be useful for the treatment of infections caused by these herpesviruses.

IT 82410-32-0, Ganciclovir
 RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (-resistant strains; in vitro activities of benzimidazole D- and L-ribonucleosides against herpesviruses)
 RN 82410-32-0 HCAPLUS
 CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[[2-hydroxy-1-(hydroxymethyl)ethoxy]methyl]- (CA INDEX NAME)

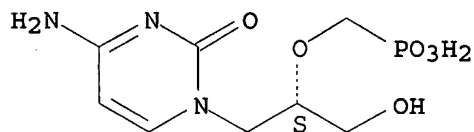


IT 59277-89-3, Acyclovir 113852-37-2, Cidofovir
 RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (comparison compound; in vitro activities of benzimidazole D- and L-ribonucleosides against herpesviruses)
 RN 59277-89-3 HCAPLUS
 CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[(2-hydroxyethoxy)methyl]- (CA INDEX NAME)



RN 113852-37-2 HCAPLUS
 CN Phosphonic acid, P-[[[(1S)-2-(4-amino-2-oxo-1(2H)-pyrimidinyl)-1-(hydroxymethyl)ethoxy]methyl]- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 5 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:484460 HCAPLUS <<LOGINID::20070502>>

DOCUMENT NUMBER: 139:374303

TITLE: Binding of a N,N'-bisheteryl derivative of dispirotripiperazine to heparan sulfate residues on the cell surface specifically prevents infection of viruses from different families

AUTHOR(S): Schmidtke, M.; Karger, A.; Meerbach, A.; Egerer, R.; Stelzner, A.; Makarov, V.

CORPORATE SOURCE: Institute of Virology and Antiviral Therapy, Friedrich Schiller University of Jena, Jena, D-07745, Germany

SOURCE: Virology (2003), 311(1), 134-143
 CODEN: VIRLAX; ISSN: 0042-6822

PUBLISHER: Elsevier Science

DOCUMENT TYPE: Journal

LANGUAGE: English

AB N,N'-bisheteryl derivs. of dispirotripiperazine (DSTP) are a novel class of antiviral compds. with some of their representatives very effectively inhibiting the replication of herpes simplex virus type 1 (HSV-1) in cell culture. Using one representative of these compds., the N,N'-bis(1-oxido[1,2,5]oxadiazolo[3,4-d]pyrimidin-7-yl)-3,12-diaza-6,9-diazonia(5,2,5,2)dispirohexadecane dichloride (DSTP 27), we here further tried to elucidate the mol. mechanisms responsible for the antiviral activity. The results from plaque reduction assays under a variety of conditions suggest that inhibition of HSV-1 strain Kupka replication by DSTP 27 occurs at the level of viral attachment by blockade of heparan sulfate (HS) structures on the cell surface that are used as viral receptors. In contrast to heparin and pentosan polysulfate, pretreatment of cells with DSTP 27 resulted in efficient inhibition of viral adsorption and replication persisting several hours after removal of the inhibitor. Specific binding of DSTP 27 to heparin was demonstrated in vitro. Titrs. of gC-pos. and gC-neg. pseudorabies virus (PrV) mutants on HS-pos. and HS-neg. cell lines confirmed that inhibitory action of DSTP 27 is strictly HS dependent. Aside from HSV-1 Kupka and PrV, DSTP 27 efficiently inhibits growth of several HSV-1 and HSV-2 strains, among them aciclovir/foscarnet-resistant strains, human cytomegalovirus, human

respiratory syncytial virus, and human immunodeficiency viruses known to attach to the cell surface via HS.

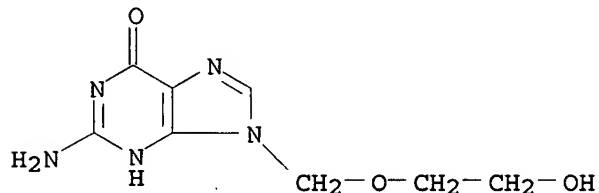
IT 59277-89-3, Aciclovir

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(aciclovir/foscarnet-resistant strains; binding of a N,N'-bisheteryl derivative of dispirotripiperazine to heparan sulfate residues on cell surface specifically prevents infection of viruses from different families)

RN 59277-89-3 HCAPLUS

CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[(2-hydroxyethoxy)methyl]- (CA INDEX NAME)



REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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SINCE FILE	TOTAL
ENTRY	SESSION
34.15	165.52

FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE	TOTAL
ENTRY	SESSION
-3.90	-14.82

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FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Apr 27, 2007 (20070427/UP).

=> d his

(FILE 'HOME' ENTERED AT 15:58:27 ON 02 MAY 2007)

FILE 'HCAPLUS' ENTERED AT 15:58:36 ON 02 MAY 2007
E US20040259832/PN 25

L1 1 S E3

FILE 'STNGUIDE' ENTERED AT 15:59:26 ON 02 MAY 2007

FILE 'HCAPLUS' ENTERED AT 16:02:09 ON 02 MAY 2007

L2 43567 S (9002-06-6 OR 4408-78-0 OR 4428-95-9 OR 59277-89-3 OR 66341-
L3 237600 S (9002-89-5 OR 9004-34-6 OR 9005-25-8 OR 9012-36-6 OR 24980-4
L4 276194 S L2 OR L3
L5 1 S L4 AND L1

FILE 'STNGUIDE' ENTERED AT 16:03:41 ON 02 MAY 2007

FILE 'HCAPLUS' ENTERED AT 16:07:58 ON 02 MAY 2007

L6 6746 S (59277-89-3 OR 66341-16-0 OR 82410-32-0 OR 86761-39-9 OR 104
E HERPES+ALL/CT
L7 2471 S L6 AND (HERPES OR "HERPES" OR "INFECTION" (L) "HERPES" OR "SK
L8 113 S ACYCLOVIR ?PHOSPHATE?
L9 40 S L8 AND L7
L10 38 S L9 AND 1800<=PY<=2003
L11 9845 S THYMIDINE KINASE
L12 24 S L11 AND L10
L13 76 S THYMIDINE KINASE INHIBITOR
L14 0 S L13 AND L12
L15 684 S CIDOFOVIR
L16 89 S L15 AND L7
L17 0 S L16 AND L10
L18 0 S GANCICLOVIR MONOPHOSPHATE
L19 3504 S GANCICLOVIR
L20 11 S GANCICLOVIR MONOPHOSPHATE
L21 2 S L20 AND L7

FILE 'STNGUIDE' ENTERED AT 16:16:23 ON 02 MAY 2007

FILE 'HCAPLUS' ENTERED AT 16:18:06 ON 02 MAY 2007

L22 3 S FORSCARNET
L23 857 S FOSCARNET
L24 121 S L23 AND L7
L25 93 S L24 AND 1800<=PY<=2003

FILE 'STNGUIDE' ENTERED AT 16:19:38 ON 02 MAY 2007

=> fil hcaplus

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

0.12

165.64

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE

TOTAL

ENTRY

SESSION

CA SUBSCRIBER PRICE

0.00

-14.82

FILE 'HCAPLUS' ENTERED AT 16:20:46 ON 02 MAY 2007

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FILE COVERS 1907 - 2 May 2007 VOL 146 ISS 19

FILE LAST UPDATED: 1 May 2007 (20070501/ED)

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L26 93 L25 AND (L20 OR L16 OR L13 OR L24 OR L10)

=> s l25 and l20

L27 0 L25 AND L20

=> s l25 and l16

L28 23 L25 AND L16

=> s l25 and l13

L29 0 L25 AND L13

=> s l25 and l24

L30 93 L25 AND L24

=> s l25 and l10

L31 1 L25 AND L10

=> d l31 ibib abs hitstr

L31 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:580763 HCAPLUS <<LOGINID::20070502>>

DOCUMENT NUMBER: 135:327001

TITLE: The potency of acyclovir can be markedly different in different cell types

AUTHOR(S): Brandi, Giorgio; Schiavano, Giuditta F.; Balestra, Emanuela; Tavazzi, Barbara; Perno, Carlo-Federico; Magnani, Mauro

CORPORATE SOURCE: Institute of Toxicologic Hygienic and Environmental Science, "G. Fornaini" University of Urbino, Urbino, Italy

SOURCE: Life Sciences (2001), 69(11), 1285-1290

CODEN: LIFSAK; ISSN: 0024-3205

PUBLISHER: Elsevier Science Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Acyclovir is an acyclic guanine analog with a considerable activity against herpes simplex viruses. We studied the antiherpetic activity of acyclovir in macrophages and fibroblast cell lines. Utilizing a plaque reduction assay we found that acyclovir potently inhibited the HSV-1 replication in macrophages (EC50 = 0.0025 μ M) compared to Vero (EC50 = 8.5 μ M) and MRC-5 (EC50 = 3.3 μ M) cells. The cytotoxicity of acyclovir was not detected at concns. \leq 20 μ M, thus the selective index in macrophages was $>$ 8000. This marked difference in antiherpetic activity between macrophages and fibroblasts was not observed with Foscarnet and PMEA. We suggest that this potent antiviral effect of acyclovir is mainly due to a proficient phosphorylation of the drug and/or a favorable dGTP/acyclovir triphosphate ratio in macrophage cells.

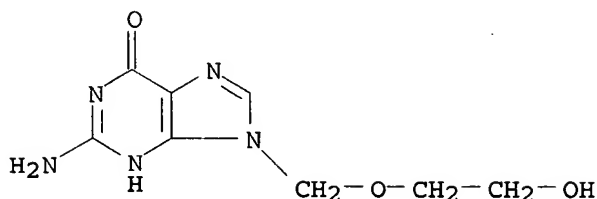
IT 59277-89-3, Acyclovir 106941-25-7, PMEA

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

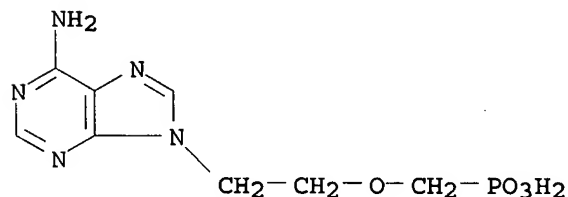
(potency of acyclovir can be markedly different in different cell types)

RN 59277-89-3 HCAPLUS

CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[(2-hydroxyethoxy)methyl]- (CA INDEX NAME)



RN 106941-25-7 HCAPLUS
 CN Phosphonic acid, P-[[2-(6-amino-9H-purin-9-yl)ethoxy)methyl]- (CA INDEX NAME)



REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d l28 ibib abs hitstr

L28 ANSWER 1 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2003:741595 HCAPLUS <<LOGINID::20070502>>
 DOCUMENT NUMBER: 140:104511
 TITLE: Comparison of HSV-1 thymidine kinase-dependent and -independent inhibition of replication-competent adenoviral vectors by a panel of drugs
 AUTHOR(S): Wildner, Oliver; Hoffmann, Dennis; Jogler, Christian; Ueberla, Klaus
 CORPORATE SOURCE: Bldg. MA, Abteilung fuer Molekulare und Medizinische Virologie, Ruhr-Universitaet Bochum, Bochum, D-44801, Germany
 SOURCE: Cancer Gene Therapy (2003), 10(10), 791-802
 CODEN: CGTHEG; ISSN: 0929-1903
 PUBLISHER: Nature Publishing Group
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Replication-competent adenoviral vectors hold the promise to be more efficient gene delivery vehicles than their replication-deficient counterparts, but they are also associated with a higher risk for adverse effects, especially in light of the fact that there is no established effective therapy for serious, disseminated adenovirus infection. To assess whether the therapeutic options to inhibit adenoviral replication can be enhanced by expressing a suicide gene, we examined the antiadenoviral effects of 15 drugs against wild-type adenovirus type 5 (Ad5) and an Ad5-based replication-competent vector expressing herpes simplex virus-1 thymidine kinase (HSV-tk) (Ad.OW34) using a real-time polymerase chain reaction -based assay and flow cytometry. Ad5 and Ad.OW34 were highly susceptible to the fluorinated pyrimidine analogs 5-fluoro-2'-deoxyuridine (FUDR), 5-fluorouridine (FUR), and trifluorothymidine (TFT), with a mean 50% inhibitory concentration (IC50) ranging from 0.12 to 0.32 µM. The mean IC50 of ribavirin and cidofovir (CDV) for Ad5, the most frequently used drugs to treat adenovirus disease,

was 6.87 and 3.19 μM , resp. In contrast to Ad5, the Ad.OW34 vector was susceptible to (E)-5-(2-bromovinyl)-2'-deoxyuridine (BVdU, IC50 0.09 μM), ganciclovir (GCV, IC50 0.19 μM), and acyclovir (ACV, IC50 32.04 μM). Addnl., we demonstrated in an animal model that Ad.OW34 vector replication can be inhibited significantly by GCV, CDV, and TFT by 35.2, 7.7, and 3.7-fold, resp., compared to untreated animals. The observed antiadenoviral effects were primarily not through cell killing, since the in vitro 50% cytotoxic concns. (CC50) were more than 1000 times higher than the antiadenoviral IC50 of the drugs examined, even in cells stably expressing HSV-tk. Since for HSV-tk-dependent inhibition of adenoviral vectors, stability of HSV-tk expression is crucial, we examined Ad.OW34 vector stability, by passaging the vector 10 times serially in the presence of 10 μM GCV. The HSV-tk/GCV system neither changed the susceptibility of Ad.OW34 to GCV significantly nor detectable vector rearrangements occurred, suggesting that the system might be suitable as a fail-safe mechanism to stop adenoviral vector replication.

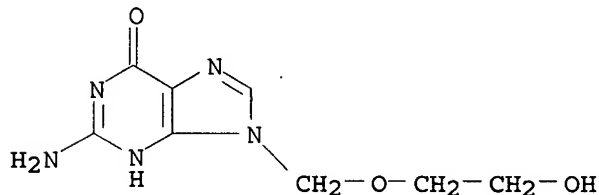
IT 59277-89-3, Acyclovir 82410-32-0, Ganciclovir
113852-37-2, Cidofovir

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)

(inhibition of replication competent adenoviral vectors by a panel of
drugs)

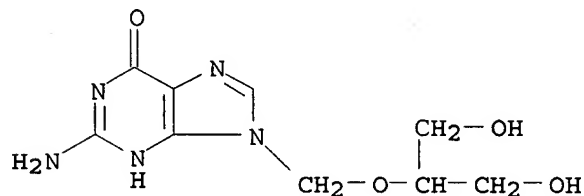
RN 59277-89-3 HCAPLUS

CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[(2-hydroxyethoxy)methyl]- (CA
INDEX NAME)



RN 82410-32-0 HCAPLUS

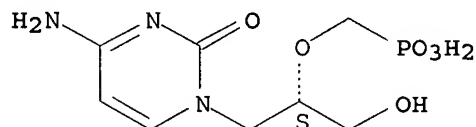
CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[[2-hydroxy-1-(hydroxymethyl)ethoxy]methyl]- (CA INDEX NAME)



RN 113852-37-2 HCAPLUS

CN Phosphonic acid, P-[[[(1S)-2-(4-amino-2-oxo-1(2H)-pyrimidinyl)-1-(hydroxymethyl)ethoxy]methyl]- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 101 THERE ARE 101 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L28 ANSWER 2 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:526763 HCAPLUS <<LOGINID::20070502>>

DOCUMENT NUMBER: 139:175724

TITLE: Drug resistance patterns of recombinant herpes simplex virus DNA polymerase mutants generated with a set of overlapping cosmids and plasmids

AUTHOR(S): Bestman-Smith, Julie; Boivin, Guy

CORPORATE SOURCE: Centre de Recherche en Infectiologie of the Centre Hospitalier Universitaire de Quebec (Pavillon CHUL) and Universite Laval, Quebec, Can.

SOURCE: Journal of Virology (2003), 77(14), 7820-7829

CODEN: JOVIAM; ISSN: 0022-538X

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Herpes simplex virus (HSV) DNA polymerase (Pol) mutations can confer resistance to all currently available antiherpetic drugs. However, discrimination between mutations responsible for drug resistance and those that are part of viral polymorphism can be difficult with current methodologies. A new system is reported for rapid generation of recombinant HSV type 1 (HSV-1) DNA Pol mutants based on transfection of a set of overlapping viral cosmids and plasmids. With this approach, twenty HSV-1 recombinants with single or dual mutations within the DNA pol gene were successfully generated and subsequently evaluated for their susceptibilities to acyclovir (ACV), foscarnet (FOS), cidofovir (CDV), and adefovir (ADV). Mutations within DNA Pol conserved regions II (A719T and S724N), VI (L778M, D780N, and L782I), and I (F891C) were shown to induce cross-resistance to ACV, FOS, and ADV, with two of these mutations (S724N and L778M) also conferring significant reduction in CDV susceptibility. Mutant F891C was associated with the highest levels of resistance towards ACV and FOS and was strongly impaired in its replication capacity. One mutation (D907V) lying outside of the conserved regions was also associated with this ACV-, FOS-, and ADV-resistant phenotype. Some mutations (K522E and Y577H) within the δ -region C were lethal, whereas others (P561S and V573M) induced no resistance to any of the drugs tested. Recombinants harboring mutations within conserved regions V (N961K) and VII (Y941H) were resistant to ACV but susceptible to FOS. Finally, mutations within conserved region III were associated with various susceptibility profiles. This new system allows a rapid and accurate evaluation of the functional role of various DNA Pol mutations, which should translate into improved management of drug-resistant HSV infections.

IT 59277-89-3, Acyclovir 106941-25-7, Adefovir

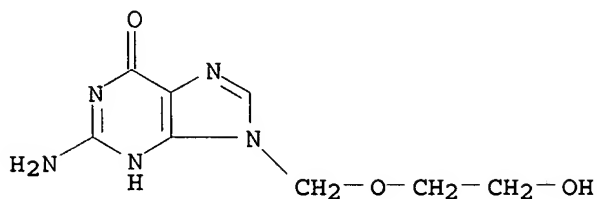
113852-37-2, Cidofovir

RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

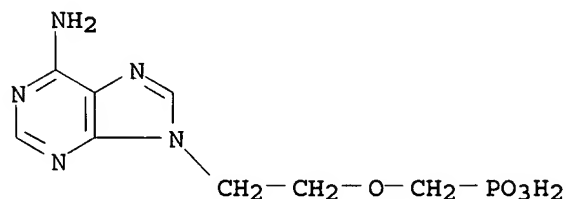
(drug resistance patterns of recombinant herpes simplex virus DNA polymerase mutants generated with a set of overlapping cosmids and plasmids)

RN 59277-89-3 HCAPLUS

CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[(2-hydroxyethoxy)methyl]- (CA INDEX NAME)

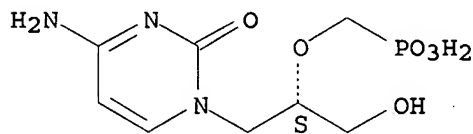


RN 106941-25-7 HCAPLUS
 CN Phosphonic acid, P-[[2-(6-amino-9H-purin-9-yl)ethoxy]methyl]- (CA INDEX NAME)



RN 113852-37-2 HCAPLUS
 CN Phosphonic acid, P-[[[(1S)-2-(4-amino-2-oxo-1(2H)-pyrimidinyl)-1-(hydroxymethyl)ethoxy]methyl]- (CA INDEX NAME)

Absolute stereochemistry.

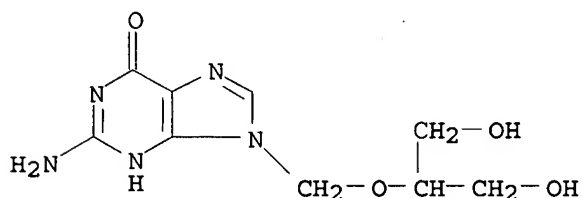


REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

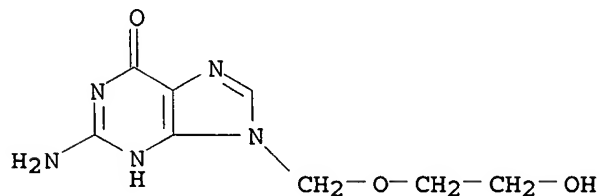
L28 ANSWER 3 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2003:513247 HCAPLUS <<LOGINID::20070502>>
 DOCUMENT NUMBER: 139:358071
 TITLE: In vitro activities of benzimidazole D- and L-ribonucleosides against herpesviruses
 AUTHOR(S): Williams, Stephanie L.; Hartline, Carroll B.; Kushner, Nicole L.; Harden, Emma A.; Bidanset, Deborah J.; Drach, John C.; Townsend, Leroy B.; Underwood, Mark R.; Biron, Karen K.; Kern, Earl R.
 CORPORATE SOURCE: University of Alabama School of Medicine, Birmingham, AL, USA
 SOURCE: Antimicrobial Agents and Chemotherapy (2003), 47(7), 2186-2192
 CODEN: AMACQ; ISSN: 0066-4804
 PUBLISHER: American Society for Microbiology
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Herpes simplex virus types 1 and 2 (HSV-1 and HSV-2), varicella-zoster virus (VZV), cytomegalovirus (CMV), Epstein-Barr virus (EBV), human herpesvirus 6 (HHV-6), and human herpesvirus 8 (HHV-8) are responsible for a number of clin. manifestations in both normal and

immunocompromised individuals. The parent benzimidazole ribonucleosides evaluated in this series, 2-bromo-5,6-dichloro-1-(β -D-ribofuranosyl)benzimidazole (BDCRB) and maribavir (1263W94), are potent and selective inhibitors of human CMV replication. These nucleosides act by two different mechanisms. BDCRB blocks the processing and maturation of viral DNA, whereas 1263W94 inhibits the viral enzyme pUL97 and interferes with DNA synthesis. In the present study, we have evaluated the in vitro antiviral activity of BDCRB, an analog, GW275175X (175X), and 1263W94 against the replication of HSV-1, HSV-2, VZV, CMV, EBV, HHV-6, and HHV-8. By using various methodologies, significant activity was observed against human CMV and EBV but not against HSV-1, HSV-2, VZV, HHV-6, or HHV-8. Plaque reduction assays performed on a variety of laboratory and clin. isolates of human CMV indicated that all strains, including those resistant to ganciclovir (GCV) and foscarnet, were sensitive to all three benzimidazole ribonucleosides, with mean 50% effective concentration values of about 1 to 5 μ M compared to that of GCV at 6 μ M. The toxicity of these compds. in tissue culture cells appeared to be similar to that observed with GCV. These results demonstrate that the benzimidazole ribonucleosides are active against human CMV and EBV and suggest that they may be useful for the treatment of infections caused by these herpesviruses.

IT 82410-32-0, Ganciclovir
 RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (-resistant strains; in vitro activities of benzimidazole D- and L-ribonucleosides against herpesviruses)
 RN 82410-32-0 HCAPLUS
 CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[[2-hydroxy-1-(hydroxymethyl)ethoxy]methyl]- (CA INDEX NAME)



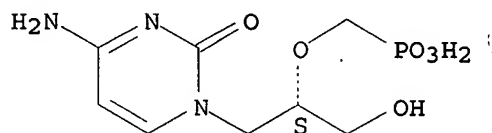
IT 59277-89-3, Acyclovir 113852-37-2, Cidofovir
 RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (comparison compound; in vitro activities of benzimidazole D- and L-ribonucleosides against herpesviruses)
 RN 59277-89-3 HCAPLUS
 CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[(2-hydroxyethoxy)methyl]- (CA INDEX NAME)



RN 113852-37-2 HCAPLUS
 CN Phosphonic acid, P-[[[(1S)-2-(4-amino-2-oxo-1(2H)-pyrimidinyl)-1-

(hydroxymethyl)ethoxy)methyl]- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 4 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:397332 HCAPLUS <<LOGINID::20070502>>

DOCUMENT NUMBER: 139:110942

TITLE: Management of acyclovir-resistant herpes simplex virus

AUTHOR(S): Chilukuri, Suneel; Rosen, Ted

CORPORATE SOURCE: Department of Dermatology, Baylor College of Medicine, Houston, TX, 77030, USA

SOURCE: Dermatologic Clinics (2003), 21(2), 311-320

CODEN: DRMCDJ; ISSN: 0733-8635

PUBLISHER: W. B. Saunders Co.

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. Acyclovir and related compds. are the mainstay of therapy of infections that are caused by human herpesvirus types I, II, and III. Resistance to this class of drugs has increased among patients who are immunocompromised (bone marrow and organ transplant patients, patients with cancer, and patients infected with HIV), leading to persistent mucocutaneous lesions or serious systemic infections. Alternative treatment regimens include parenteral foscarnet, vidarabine, and cidofovir, as well as topical foscarnet, cidofovir, trifluridine, and imiquimod. Ribonucleotide reductase inhibitors offer considerable promise for future treatment.

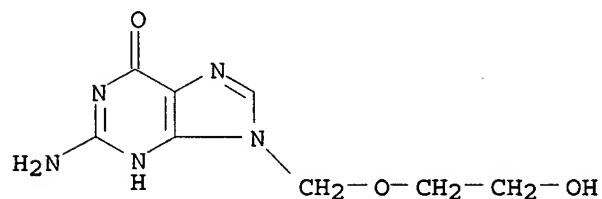
IT 59277-89-3, Acyclovir 113852-37-2, Cidofovir

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(management of acyclovir-resistant herpes simplex virus)

RN 59277-89-3 HCAPLUS

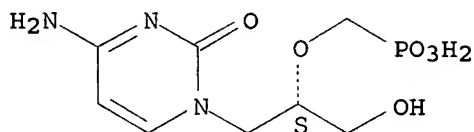
CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[(2-hydroxyethoxy)methyl]- (CA INDEX NAME)



RN 113852-37-2 HCAPLUS

CN Phosphonic acid, P-[[[(1S)-2-(4-amino-2-oxo-1(2H)-pyrimidinyl)-1-(hydroxymethyl)ethoxy)methyl]- (CA INDEX NAME)

Absolute stereochemistry.

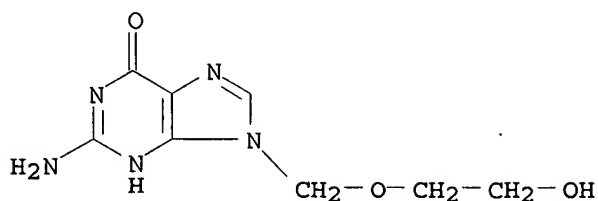


REFERENCE COUNT: 122 THERE ARE 122 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 5 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2003:102544 HCAPLUS <<LOGINID::20070502>>
 DOCUMENT NUMBER: 139:269931
 TITLE: Herpes simplex virus resistance to antiviral drugs
 AUTHOR(S): Morfin, Florence; Thouvenot, Danielle
 CORPORATE SOURCE: 8 avenue Rockefeller, Domaine Rockefeller, Laboratory of Virology of the Hospices Civils de Lyon, Lyon, 69373, Fr.
 SOURCE: Journal of Clinical Virology (2003), 26(1), 29-37
 CODEN: JCVIFB; ISSN: 1386-6532
 PUBLISHER: Elsevier Science Ltd.
 DOCUMENT TYPE: Journal; General Review
 LANGUAGE: English

AB A review. Herpes simplex virus (HSV) infections are efficiently treated with antiviral drugs such as acyclovir (ACV). However, resistance has been reported, mainly among immunocompromised patients (prevalence around 5%) and particularly allogeneic bone marrow transplant patients (prevalence reaching 30%). Resistance to ACV is associated with mutations on one of the two viral enzymes involved in the ACV mechanism of action: thymidine kinase (TK) and DNA polymerase. In 95% of the cases, ACV resistance is associated with a mutation in the TK gene as this enzyme is not essential for viral replication, unlike viral DNA polymerase, which is rarely involved in resistance. Strains resistant to ACV are almost always cross-resistant to other TK-dependent drugs such as penciclovir and famciclovir. Resistant infections can be managed by foscarnet or cidofovir but both are more toxic than ACV. These drugs also inhibit viral DNA polymerase but they are active on most ACV-resistant HSV as they do not depend on TK; nevertheless virus resistant to ACV because of a mutation in the DNA polymerase may be cross-resistant to these mols. Published data on genetic characterization of resistant clin. isolates point out hot spots in viral TK and DNA polymerase genes. TK mutations associated with resistance are either insertion or deletion (codons 92 and 146 of TK gene) or substitution (codon 176-177, 336 of TK gene). DNA polymerase mutations are mainly located in conserved sites of the enzyme. A high level of gene polymorphism has also been reported for these genes, especially for TK. These results are useful for the development of rapid genotypic assays for the detection of mutations associated with resistance.

IT 59277-89-3, Acyclovir
 RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (herpes simplex virus resistance to antiviral drugs)
 RN 59277-89-3 HCAPLUS
 CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[(2-hydroxyethoxy)methyl]- (CA INDEX NAME)

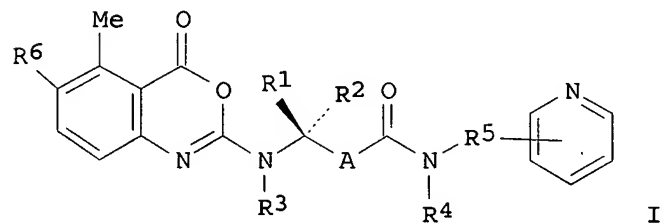


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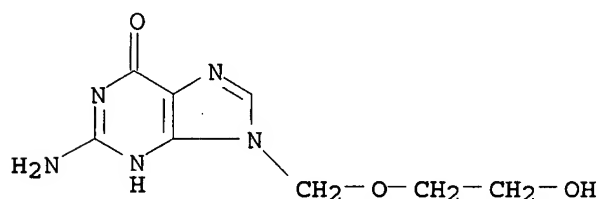
L28 ANSWER 6 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2003:22872 HCAPLUS <<LOGINID::20070502>>
 DOCUMENT NUMBER: 138:89816
 TITLE: Preparation of pyridine ring-containing benzoxazinone derivatives for treatment of viral infections
 INVENTOR(S): Takahashi, Wataru; Watanabe, Naoto; Saito, Yasuyoshi
 PATENT ASSIGNEE(S): Asahi Kasei Kabushiki Kaisha, Japan
 SOURCE: PCT Int. Appl., 104 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003002558	A1	20030109	WO 2002-JP5795	20020611 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002306312	A1	20030303	AU 2002-306312	20020611 <--
EP 1403269	A1	20040331	EP 2002-733468	20020611
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2004116420	A1	20040617	US 2003-480451	20031212
PRIORITY APPLN. INFO.:			JP 2001-179282	A 20010613
			JP 2001-379282	A 20011212
			WO 2002-JP5795	W 20020611

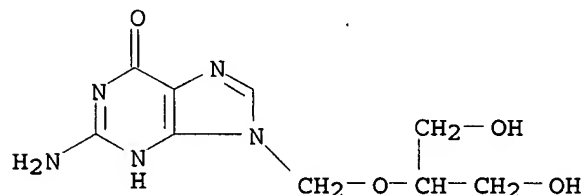
OTHER SOURCE(S): MARPAT 138:89816
 GI



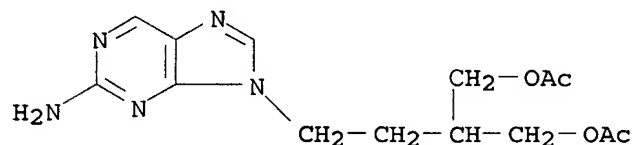
- AB The title compds. I [R1, R2 = H, alkyl, etc.; or R1CR2 = cycloalkyl; A = (CH2)n; n = 0 or 1; R3 = H, alkyl, etc.; R4 = H, alkyl, alkenyl, etc.; R5 = alkylene; or NR4R5 = heterocyclyl; R6 = H, halo, etc.] are prepared I have excellent protease inhibitory activity. I are useful in the treatment of viral infectious diseases, in particular herpesvirus infections. Compds. of this invention in vitro showed EC90 values of 3.2 μ M to > 12 μ M against HSV-1.
- IT 59277-89-3, Aciclovir 82410-32-0, Ganciclovir
104227-87-4, Famciclovir 113852-37-2, Cidofovir
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination of antiviral pyridine ring-containing benzoxazinone derivs. and another antiviral agent)
- RN 59277-89-3 HCAPLUS
- CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[(2-hydroxyethoxy)methyl]- (CA INDEX NAME)



- RN 82410-32-0 HCAPLUS
- CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[[2-hydroxy-1-(hydroxymethyl)ethoxy]methyl]- (CA INDEX NAME)

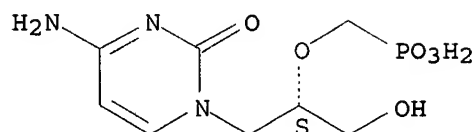


- RN 104227-87-4 HCAPLUS
- CN 1,3-Propanediol, 2-[2-(2-amino-9H-purin-9-yl)ethyl]-, 1,3-diacetate (CA INDEX NAME)



- RN 113852-37-2 HCAPLUS
- CN Phosphonic acid, P-[[[(1S)-2-(4-amino-2-oxo-1(2H)-pyrimidinyl)-1-(hydroxymethyl)ethoxy]methyl]- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 7 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:822158 HCAPLUS <<LOGINID::20070502>>

DOCUMENT NUMBER: 138:183762

TITLE: Genotypic and phenotypic characterization of the thymidine kinase of ACV-resistant HSV-1 derived from an acyclovir-sensitive herpes simplex virus type 1 strain

AUTHOR(S): Saijo, Masayuki; Suzutani, Tatsuo; De Clercq, Erik; Niikura, Masahiro; Maeda, Akihiko; Morikawa, Shigeru; Kurane, Ichiro

CORPORATE SOURCE: Department of Virology 1, Special Pathogens Laboratory, National Institute of Infectious Diseases, Musashimurayama, Tokyo, 208-0011, Japan

SOURCE: Antiviral Research (2002), 56(3), 253-262
CODEN: ARSRDR; ISSN: 0166-3542

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

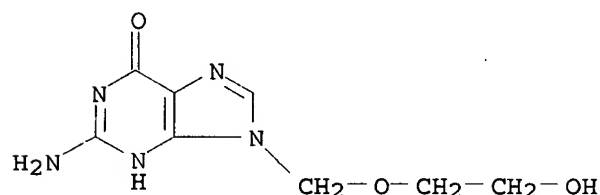
AB Twenty-four strains of acyclovir (ACV)-resistant (ACVr) herpes simplex virus type 1 (HSV-1) were generated from the HSV-1 TAS strain by exposure to ACV, and the genotype and phenotype of the thymidine kinase (TK) from these mutants were analyzed. The TK polypeptide of the ACVr HSV-1 strains was examined by Western blot using an anti-HSV-1 TK rabbit serum. The sensitivity of each strain to ACV, foscarnet and cidofovir (CDV) was also determined. A single guanine (G) insertion or a single cytosine (C) deletion was detected in 12 of the 24 ACVr strains at the G or C homopolymer stretches within the TK gene. Genotypic anal. predicted that two thirds of the ACVr HSV-1 strains expressed truncated TK polypeptides, while one third expressed viral TK polypeptide with a single amino acid substitution at various sites. Western blot abnormalities in the viral TK polypeptides were identified in 21 ACVr strains. There was an inverse correlation between the susceptibility of the HSV-1 mutant strains to ACV and that to CDV. Nucleotide sequencing of the TK gene and Western blot anal. of the viral TK polypeptides are considered to be one of the methods for predicting virus sensitivity to ACV and CDV.

IT 59277-89-3, Acyclovir

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ACV; genotypic and phenotypic characterization of thymidine kinase of acyclovir-resistant herpes simplex virus derived from acyclovir-sensitive HSV-1 strain)

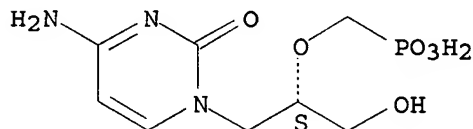
RN 59277-89-3 HCAPLUS

CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[(2-hydroxyethoxy)methyl]- (CA INDEX NAME)



IT 113852-37-2, Cidofovir
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (CDV, correlation between susceptibility of HSV-1 mutant strains to ACV
 and; genotypic and phenotypic characterization of thymidine kinase of
 acyclovir-resistant herpes simplex virus derived from
 acyclovir-sensitive HSV-1 strain)
 RN 113852-37-2 HCAPLUS
 CN Phosphonic acid, P-[[[(1S)-2-(4-amino-2-oxo-1(2H)-pyrimidinyl)-1-
 (hydroxymethyl)ethoxy]methyl]- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 8 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STM
 ACCESSION NUMBER: 2002:72315 HCAPLUS <<LOGINID::20070502>>
 DOCUMENT NUMBER: 136:129036
 TITLE: Method of screening 4-hydroxyquinolin (4-HQ),
 4-oxo-dihydroquinoline (4-oxo-DHQ), and
 4-oxo-dihydrothienopyridine (4-oxo-DHTP) derivatives
 as non-nucleoside herpesvirus DNA polymerase inhibitor
 INVENTOR(S): Homa, Fred L.; Wathen, Michael W.; Hopkins, Todd A.;
 Thomsen, Darrel R.
 PATENT ASSIGNEE(S): Pharmacia & Upjohn Company, USA
 SOURCE: PCT Int. Appl., 126 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002006513	A2	20020124	WO 2001-US16525	20010713 <--
WO 2002006513	A3	20030123		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2002076789	A1	20020620	US 2001-904065	20010712 <--
US 6682892	B2	20040127		
AU 2001072920	A5	20020130	AU 2001-72920	20010713 <--
US 2004115623	A1	20040617	US 2003-692556	20031024
PRIORITY APPLN. INFO.:				
			US 2000-218118P	P 20000713
			US 2001-283880P	P 20010413
			US 2001-904065	A3 20010712
			WO 2001-US16525	W 20010713
AB The present invention provides a method for selecting non-nucleoside				

herpesvirus DNA polymerase inhibitors from 4-HQ, 4-oxo-DHQ, and 4-oxo-DHTP derivs. by measuring IC50. The invention also provides sequences of mutant herpesvirus DNA polymerase genes which resist non-nucleoside inhibitors, and herpesvirus mutant strains containing the drug-resistant DNA polymerase genes. The present invention relates to a method for selecting an anti-herpes viral compound and a method for selectively inhibiting herpesvirus in a human host in need of such treatment. The present invention relates to a method for selecting an anti-herpes viral compound and a method for selectively inhibiting herpesvirus in a human host in need of such treatment.

IT 59277-89-3, Acyclovir 82410-32-0, Ganciclovir

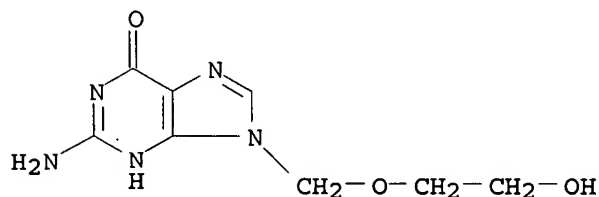
113852-37-2, Cidofovir

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(4-HQ, 4-oxo-DHQ, and 4-oxo-DHTP derivs. as non-nucleoside herpesvirus DNA polymerase inhibitor)

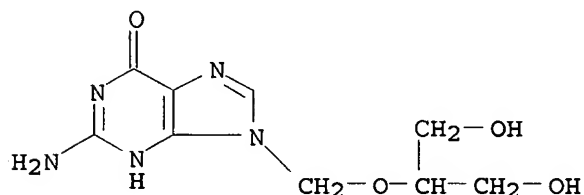
RN 59277-89-3 HCAPLUS

CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[(2-hydroxyethoxy)methyl]- (CA INDEX NAME)



RN 82410-32-0 HCAPLUS

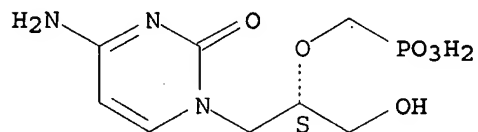
CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[[2-hydroxy-1-(hydroxymethyl)ethoxy]methyl]- (CA INDEX NAME)



RN 113852-37-2 HCAPLUS

CN Phosphonic acid, P-[[[(1S)-2-(4-amino-2-oxo-1(2H)-pyrimidinyl)-1-(hydroxymethyl)ethoxy]methyl]- (CA INDEX NAME)

Absolute stereochemistry.



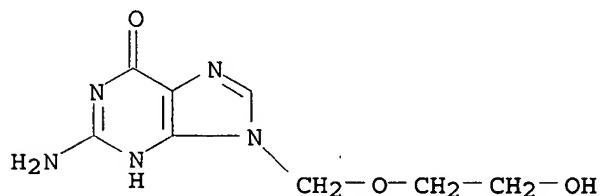
L28 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:825249 HCAPLUS <<LOGINID::20070502>>

DOCUMENT NUMBER: 136:318855
 TITLE: Infection due to aciclovir resistant
 herpes simplex virus in patients undergoing
 allogeneic hematopoietic stem cell transplantation
 AUTHOR(S): Venard, V.; Dauendorffer, J. N.; Carret, A. S.;
 Corsaro, D.; Edert, D.; Bordigoni, P.; Le Faou, A.
 CORPORATE SOURCE: Unite mixte de recherche 7565 UHP-CNRS, laboratoire de
 bacteriologie-virologie, faculte de medecine,
 Vandoeuvre-les-Nancy, Fr.
 SOURCE: Pathologie Biologie (2001), 49(7), 553-558
 CODEN: PTBIAN; ISSN: 0031-3009
 PUBLISHER: Editions Scientifiques et Medicales Elsevier
 DOCUMENT TYPE: Journal
 LANGUAGE: English

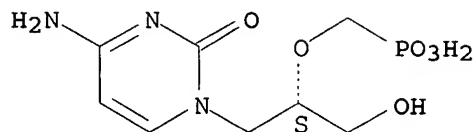
AB Over an 8-mo period from Oct. 1997 to May 1998, 4 patients who had
 received bone marrow transplant (BMT) from unrelated donor presented with
 severe mucosal cutaneous infections involving aciclovir
 resistant herpes simplex virus 1 (HSV-1). The 4 isolates were
 aciclovir (ACV) resistant, 3 of which were also foscarnet
 resistant as determined by the dye uptake method. The sequencing of the
 thymidine kinase (TK) gene did not permit to establish a relation between
 mutations and resistance to ACV. 3 Patients were considered as clin.
 cured of their HSV infection by replacement of ACV or
 foscarnet with either valaciclovir (1 case) or cidofovir
 (two cases) but eventually 2 of them died of graft vs host disease. 1
 Patient died of extensive HSV infection despite administration
 of cidofovir. This study emphasizes the importance of
 monitoring the herpes virus resistance to antiviral drugs in
 bone marrow transplant recipients and the usefulness of the evaluation of
 novel antiviral drug for treatment of infections due to strains
 of HSV resistant to ACV and foscarnet that occur in about 5% of
 immunocompromised patients.

IT 59277-89-3, Aciclovir
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (aciclovir resistant herpes simplex virus infection
 in patients undergoing allogeneic hematopoietic stem cell
 transplantation)
 RN 59277-89-3 HCAPLUS
 CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[(2-hydroxyethoxy)methyl]- (CA
 INDEX NAME)



IT 113852-37-2, Cidofovir
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (antiviral therapy of aciclovir resistant HSV infection in patients
 undergoing allogeneic hematopoietic stem cell transplantation)
 RN 113852-37-2 HCAPLUS
 CN Phosphonic acid, P-[[{(1S)-2-(4-amino-2-oxo-1(2H)-pyrimidinyl)-1-(
 hydroxymethyl)ethoxy)methyl]- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 10 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:223450 HCAPLUS <<LOGINID::20070502>>

DOCUMENT NUMBER: 135:174514

TITLE: Prophylaxis against herpesvirus infections in transplant recipients

AUTHOR(S): Ljungman, Per

CORPORATE SOURCE: Department of Haematology, Karolinska Institutet, Huddinge University Hospital, Huddinge, Swed.

SOURCE: Drugs (2001), 61(2), 187-196

CODEN: DRUGAY; ISSN: 0012-6667

PUBLISHER: Adis International Ltd.

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review with 63 refs. Herpesvirus infections are important after stem cell and organ transplant. During the last decades several antiviral agents have been introduced with efficacy against herpesviruses. These agents are the nucleoside analogs acyclovir, valaciclovir, famciclovir, and ganciclovir; the nucleotide analog cidofovir; and the pyrophosphate analog foscarnet. Several studies have been performed with antiviral agents with the aim to reduce morbidity and mortality associated with herpesvirus infections in transplant recipients. Aciclovir and valaciclovir have been examined in randomized, controlled trials in both solid organ and stem cell transplant patients, and were shown to be very effective for the prevention of herpes simplex virus (HSV) and varicella-zoster virus infections. In addition, these drugs were shown to reduce cytomegalovirus (CMV) infection and improve survival in allogenic stem cell transplant patients and to reduce CMV infection, CMV disease (aciclovir and valaciclovir), and acute rejection (valaciclovir) in renal transplant patients. Ganciclovir is very effective for the prevention of CMV infection and disease in both stem cell and solid organ transplant recipients. It can also be used in preemptive strategies in which the aim is to prevent CMV disease in patients who have ongoing CMV infection documented by antigenemia or detection of CMV DNA. The latter strategy has the advantage of reducing the exposure to the drug and thereby the risk for toxicity. Foscarnet has also been shown to be effective as preemptive therapy for CMV in allogenic stem cell transplant patients and as therapy for aciclovir-resistant HSV infections. Finally cidofovir is an interesting agent with broad spectrum antiherpes virus efficacy. However, because of the drug's toxicity profile, further studies are needed.

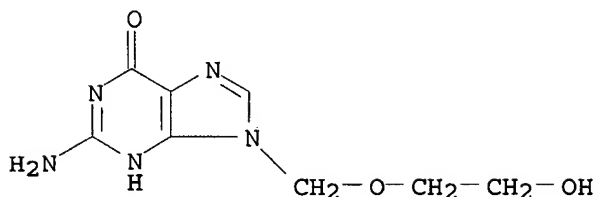
IT 59277-89-3, Aciclovir 82410-32-0, Ganciclovir 104227-87-4, Famciclovir 113852-37-2, Cidofovir

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

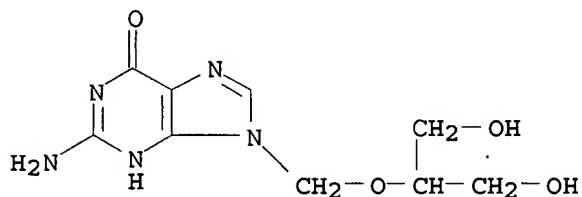
(prophylaxis against herpesvirus infections in transplant recipients)

RN 59277-89-3 HCAPLUS

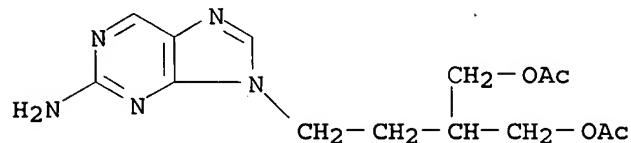
CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[(2-hydroxyethoxy)methyl]- (CA INDEX NAME)



RN 82410-32-0 HCAPLUS
CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[[2-hydroxy-1-(hydroxymethyl)ethoxy]methyl]- (CA INDEX NAME)

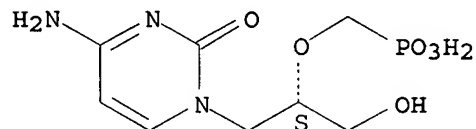


RN 104227-87-4 HCAPLUS
CN 1,3-Propanediol, 2-[2-(2-amino-9H-purin-9-yl)ethyl]-, 1,3-diacetate (CA INDEX NAME)



RN 113852-37-2 HCAPLUS
CN Phosphonic acid, P-[[[(1S)-2-(4-amino-2-oxo-1(2H)-pyrimidinyl)-1-(hydroxymethyl)ethoxy]methyl]- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 11 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:41285 HCAPLUS <<LOGINID::20070502>>
DOCUMENT NUMBER: 135:116203
TITLE: Current recommendations for the treatment of genital herpes
AUTHOR(S): Leung, Daniel T.; Sacks, Stephen L.
CORPORATE SOURCE: Wake Forest University School of Medicine, Winston Salem, NC, USA

SOURCE: Drugs (2000), 60(6), 1329-1352
 CODEN: DRUGAY; ISSN: 0012-6667
 PUBLISHER: Adis International Ltd.
 DOCUMENT TYPE: Journal; General Review
 LANGUAGE: English

AB A review with 228 refs. The incidence of genital herpes continues to increase in epidemic-like fashion. Aciclovir (acyclovir) has been the original gold standard of therapy. The recent addition of famciclovir and valaciclovir as antiherpes drugs has improved convenience as well as the efficacy of treatment. Although aciclovir remains a widely prescribed and reliable drug, its administration schedule falls short of the ease of usage that the newer nucleoside analogs offer, for both episodic and suppressive therapy. Suppression of symptomatic disease and asymptomatic shedding from the genitalia have both become popular approaches, if not the primary targets of antiviral therapy. Knowing that asymptomatic disease leads to most cases of transmission strongly suggests that suppression with antiviral agents could reduce transmission risk in discordant couples. Unfortunately, the role for antivirals in reducing transmission remains to be proven in clin. trials. Neonatal herpes is now successfully treated using aciclovir. Current randomized clin. trials are examining aciclovir and valaciclovir administration, as well as safety and efficacy for post-acute suppressive therapy. Prevention of recurrences in pregnancy is also a topic under investigation, with a view to reducing the medical need for Cesarean section, or alternatively (and far less likely to be accomplished) to protect the neonate. Although resistance is largely limited to the immunocompromised and a change in resistance patterns is not expected, several drugs are available for the treatment of aciclovir-resistant strains of herpes simplex. Foscarnet is the main alternative with proven efficacy in this setting. Unfortunately, administration of foscarnet requires i.v. therapy, although a single anecdote of topical foscarnet efficacy in this setting has been published. Alternatives include cidofovir gel, which is not com. available but can be formulated locally from the i.v. preparation. Less effective alternatives include trifluridine and interferon. Future possibilities for treatment of genital herpes include a microparticle-based controlled-release formulation of aciclovir and resiquimod (VML-600; R-848). The search for an effective therapeutic vaccine for genital herpes has not been successful to date, although a live virus glycoprotein H-deficient (DISC) vaccine is currently in clin. trials. Recent data suggest that seroneg. women are protected (albeit, not fully) by a glycoprotein D recombinant vaccine with adjuvant. Despite the established safety and convenience of current treatment options, better suppressive options and topical treatment options are much needed. Studies using existing agents as potential tools to avoid Cesarean section, or transmission to neonate or partner are ongoing. Both vaccines and antivirals may eventually play a role in prevention of infection.

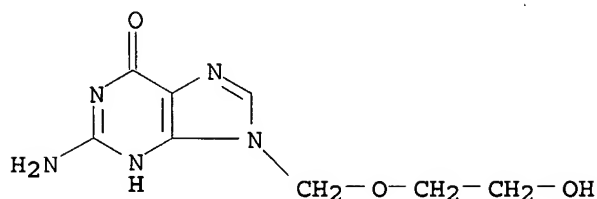
IT 59277-89-3, Aciclovir 104227-87-4, Famciclovir 113852-37-2, Cidofovir

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

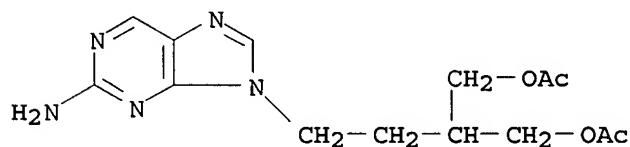
(current recommendations for treatment of genital herpes in humans)

RN 59277-89-3 HCAPLUS

CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[(2-hydroxyethoxy)methyl]- (CA INDEX NAME)

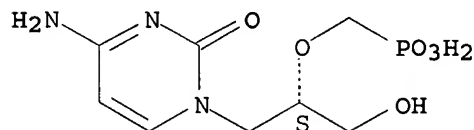


RN 104227-87-4 HCAPLUS
 CN 1,3-Propanediol, 2-[2-(2-amino-9H-purin-9-yl)ethyl]-, 1,3-diacetate (CA INDEX NAME)



RN 113852-37-2 HCAPLUS
 CN Phosphonic acid, P-[[[(1S)-2-(4-amino-2-oxo-1(2H)-pyrimidinyl)-1-(hydroxymethyl)ethoxy]methyl]- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 228 THERE ARE 228 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 12 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2000:504602 HCAPLUS <<LOGINID::20070502>>
 DOCUMENT NUMBER: 133:232393
 TITLE: Resistance to antiviral drugs in herpes simplex virus infections among allogeneic stem cell transplant recipients: risk factors and prognostic significance
 AUTHOR(S): Chakrabarti, Suparno; Pillay, Deenan; Ratcliffe, Daina; Cane, Patricia A.; Collingham, Kathryn E.; Milligan, Donald W.
 CORPORATE SOURCE: Department of Haematology, University of Birmingham Medical School, Birmingham, B9 5SS, UK
 SOURCE: Journal of Infectious Diseases (2000), 181(6), 2055-2058
 CODEN: JIDIAQ; ISSN: 0022-1899
 PUBLISHER: University of Chicago Press
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Herpes simplex virus (HSV) infections in 75 allogeneic stem cell transplant recipients were analyzed. Sixteen patients developed HSV disease following transplantation. The risk factors were age, sex (females), unrelated donor graft, and graft-vs.-host disease (GVHD) grade

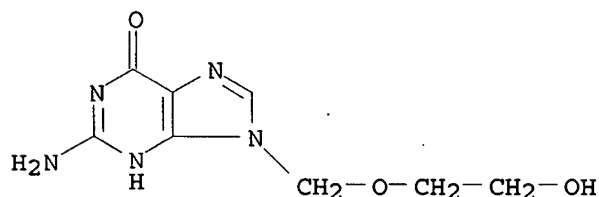
≥2. Seven patients did not respond to acyclovir, and 3 patients failed to respond to foscarnet. Isolates from 4 patients developed resistance to acyclovir/penciclovir, and 3 patients had foscarnet-resistant isolates. The remaining 3 patients failed to respond to acyclovir, despite having sensitive isolates. All the isolates were sensitive to cidofovir, for which the IC50 values correlated inversely with those for acyclovir (P = .01). The risk factors for clin. resistance to antiviral drugs were a GVHD grade ≥2 (P = .001) and the lack of ganciclovir prophylaxis (P = .01), with a higher nonrelapse mortality in the latter group (P < .0001). Clin. as well as in vitro resistance to antiviral drugs is common in patients with severe GVHD and is associated with a poor outcome.

IT 59277-89-3, Acyclovir 82410-32-0, Ganciclovir
113852-37-2, Cidofovir

RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(resistance to antiviral drugs in herpes simplex virus infections among allogeneic stem cell transplant recipients)

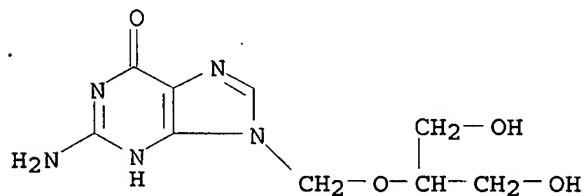
RN 59277-89-3 HCAPLUS

CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[(2-hydroxyethoxy)methyl]- (CA INDEX NAME)



RN 82410-32-0 HCAPLUS

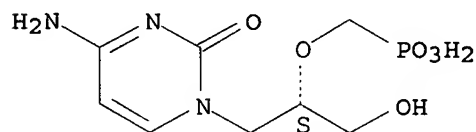
CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[[2-hydroxy-1-(hydroxymethyl)ethoxy]methyl]- (CA INDEX NAME)



RN 113852-37-2 HCAPLUS

CN Phosphonic acid, P-[[[(1S)-2-(4-amino-2-oxo-1(2H)-pyrimidinyl)-1-(hydroxymethyl)ethoxy]methyl]- (CA INDEX NAME)

Absolute stereochemistry.



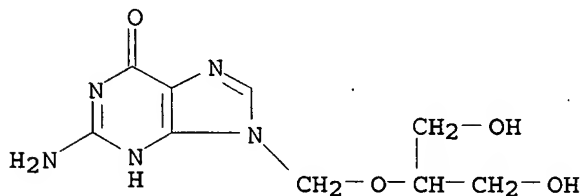
REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 13 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2000:255804 HCAPLUS <<LOGINID::20070502>>
 DOCUMENT NUMBER: 133:83919
 TITLE: Antiviral activity of ganciclovir elaidic acid ester against herpesviruses
 AUTHOR(S): Andrei, G.; Snoeck, R.; Neyts, J.; Sandvold, M. L.; Myhren, F.; De Clercq, E.
 CORPORATE SOURCE: K.U. Leuven, Rega Institute for Medical Research, Louvain, B-3000, Belg.
 SOURCE: Antiviral Research (2000), 45(3), 157-167
 CODEN: ARSRDR; ISSN: 0166-3542
 PUBLISHER: Elsevier Science B.V.
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB A fatty acid derivative of ganciclovir (GCV), elaidic acid ganciclovir (E-GCV), has been evaluated for its inhibitory activity against laboratory and clin. strains of herpes simplex type 1 (HSV-1) and type 2 (HSV-2), varicella-zoster virus (VZV) and human cytomegalovirus (HCMV) in human embryonic lung fibroblasts. GCV, cidofovir, acyclovir (ACV), brivudin (BVDU) and foscarnet (PFA) were included as reference compds. The viruses studied were wild-type, thymidine kinase-deficient (TK-) and PFA-resistant (PFAR) HSV strains. The IC50 values obtained for E-GCV were 5- to 30-fold lower than those observed for GCV, the IC50 value of E-GCV for HSV-1 strain KOS being 0.07 nM. A similarly increased activity of E-GCV (as compared to GCV) was noted for TK- and PFAR HSV-1 or HSV-2 strains. However, E-GCV did not exhibit superior activity over GCV to VZV or HCMV in vitro. The antiviral efficacy of E-GCV was also evaluated in vivo against intracerebral HSV-2 infection in NMRI mice. Animals were treated i.p. or perorally with E-GCV, GCV or placebo once daily for 10 days, starting the day of infection. E-GCV compared to GCV at equimolar doses, proved markedly more efficacious than GCV in terms of reduction of mortality rate and delay of mean time of death. The elaidic acid ester of GCV should therefore be considered as a novel approach towards the treatment of HSV infections.

IT 82410-32-0, Ganciclovir
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (antiviral activity of ganciclovir elaidic acid ester against herpesviruses)

RN 82410-32-0 HCAPLUS
 CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[[2-hydroxy-1-(hydroxymethyl)ethoxy]methyl]- (CA INDEX NAME)



REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

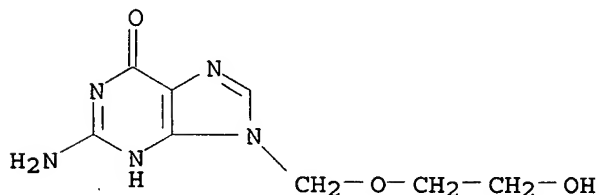
L28 ANSWER 14 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2000:161933 HCAPLUS <<LOGINID::20070502>>

DOCUMENT NUMBER: 132:303023
 TITLE: Resistance of herpes simplex virus type 1 against different phosphonylmethoxyalkyl derivatives of purines and pyrimidines due to specific mutations in the viral DNA polymerase gene
 AUTHOR(S): Andrei, Graciela; Snoeck, Robert; De Clercq, Erik; Esnouf, Robert; Fiten, Pierre; Opdenakker, Ghislain
 CORPORATE SOURCE: Laboratory of Antiviral Chemotherapy, Rega Institute for Medical Research, Katholieke Universiteit Leuven, Louvain, B-3000, Belg.
 SOURCE: Journal of General Virology (2000), 81(3), 639-648
 CODEN: JGVIAY; ISSN: 0022-1317
 PUBLISHER: Society for General Microbiology
 DOCUMENT TYPE: Journal
 LANGUAGE: English

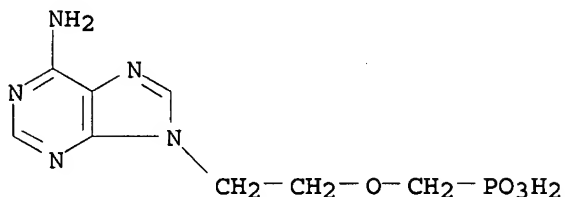
AB Drug-resistant strains of herpes simplex virus type 1 (HSV-1) were selected under the pressure of (S)-3-hydroxy-2-phosphonylmethoxypropyl (HPMP) derivs. of cytosine (HPMPC, cidofovir) and adenine (HPMPA) and 2-phosphonylmethoxyethyl (PME) derivs. of adenine (PMEA, adefovir) and 2,6-diaminopurine (PMEDAP). HPMP-resistant (HPMPCr) and HPMPAr strains were cross-resistant to one another, but they remained sensitive to foscarnet (PFA), acyclovir (ACV) and the PME derivs., while the PMEAR and PMEDAPr strains showed cross-resistance to PFA and ACV. The PMEAR, PMEDAPr and PFAr mutants all revealed a single nucleotide change resulting in a Ser-724 to Asn mutation within the conserved region II of the DNA polymerase. Two HPMPAr clones and one HPMPCr clone possessed single amino acid changes in the DNA polymerase (HPMPAr clone D1, Leu-1007 to Met; HPMPAr clone B5, Ile-1028 to Thr; HPMPCr clone C3, Val-573 to Met). The HPMPCr clone A4 contained two mutations, Ala-136 to Thr and Arg-700 to Met. The mutation at position 136, located outside the catalytic domain of the enzyme, was not detected in other HPMPCr clones, suggesting that this mutation may not be responsible for the resistant phenotype. Residue 573 is located within the 3' → 5' exonuclease editing domain close to the catalytically important residues Tyr-577 and Asp-581. Similarly, residue 700 is located in the palm subdomain of the catalytic domain, adjacent to the Asp residues 717, 886 and 888 that are vital for polymerase activity. The HPMPAr mutations at residues 1007 and 1028, beyond the last conserved region, still fall within the thumb subdomain of the catalytic domain. The different drug-resistant mutants varied in neurovirulent behavior, the HPMPCr strains showing reduced neurovirulence compared with the wild-type.

IT 59277-89-3, Acyclovir 106941-25-7, Adefovir 113852-37-2, Cidofovir
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (resistance of herpes simplex virus type 1 against different phosphonylmethoxyalkyl derivs. of purines and pyrimidines due to specific mutations in viral DNA polymerase gene)

RN 59277-89-3 HCAPLUS
 CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[(2-hydroxyethoxy)methyl]- (CA INDEX NAME)

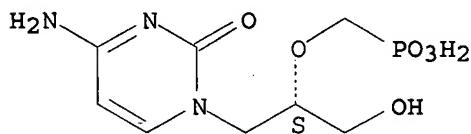


RN 106941-25-7 HCAPLUS
 CN Phosphonic acid, P-[[2-(6-amino-9H-purin-9-yl)ethoxy]methyl]- (CA INDEX NAME)



RN 113852-37-2 HCAPLUS
 CN Phosphonic acid, P-[[[(1S)-2-(4-amino-2-oxo-1(2H)-pyrimidinyl)-1-(hydroxymethyl)ethoxy]methyl]- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 15 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2000:13232 HCAPLUS <<LOGINID::20070502>>
 DOCUMENT NUMBER: 132:216381
 TITLE: Advances in the research on new antiherpesvirus drugs
 AUTHOR(S): Rostkowska-Nadolska, Beata
 CORPORATE SOURCE: Katedra i Klinika Otolaryngologii, Akademia Medyczna, Wroclaw, 51685, Pol.
 SOURCE: Postepy Higieny i Medycyny Doswiadczalnej (1999), 53(5), 675-687
 CODEN: PHMDAD; ISSN: 0032-5449
 PUBLISHER: Wydawnictwo Continuo
 DOCUMENT TYPE: Journal; General Review
 LANGUAGE: Polish

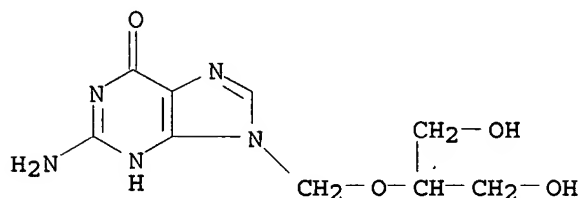
AB A review with 31 refs. Significant advances have been made in the development of effective antiherpesvirus chemotherapy in recent decades. Acyclovir was approved for the treatment of herpes simplex virus infections over 15 yr ago and it remains an important and reliable antiviral agent. The most promising new antiviral drugs are described, including purine nucleoside analogs (vidarabine, penciclovir, famciclovir, ganciclovir, valaciclovir, lobucavir), pyrimidine nucleotide analogs (epervudine, sorivudine, cidofovir), Na foscarnet, docosanol, and vrazizoline (denotivir). Focus is on drugs that have just entered the therapeutic use or are under clin. investigation and may become available shortly. The antiviral activity, results of clin. trials, and adverse side-effects are discussed.

IT 82410-32-0, Ganciclovir 104227-87-4, Famciclovir 113852-37-2, Cidofovir

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (virucides against herpes virus infections and recent research advances)

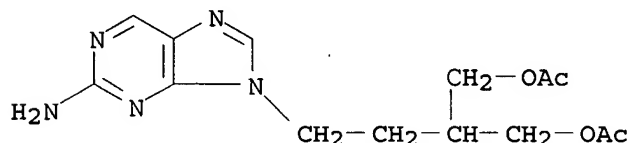
RN 82410-32-0 HCAPLUS

CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[[2-hydroxy-1-(hydroxymethyl)ethoxy]methyl]- (CA INDEX NAME)



RN 104227-87-4 HCAPLUS

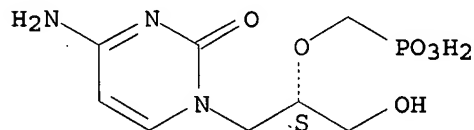
CN 1,3-Propanediol, 2-[2-(2-amino-9H-purin-9-yl)ethyl]-, 1,3-diacetate (CA INDEX NAME)



RN 113852-37-2 HCAPLUS

CN Phosphonic acid, P-[[[(1S)-2-(4-amino-2-oxo-1(2H)-pyrimidinyl)-1-(hydroxymethyl)ethoxy]methyl]- (CA INDEX NAME)

Absolute stereochemistry.



L28 ANSWER 16 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:528343 HCAPLUS <<LOGINID::20070502>>

DOCUMENT NUMBER: 132:87784

TITLE: Characterization of the DNA polymerase and thymidine kinase genes of herpes simplex virus isolates from AIDS patients in whom acyclovir and foscarnet therapy sequentially failed

AUTHOR(S): Schmit, Isabelle; Boivin, Guy

CORPORATE SOURCE: Infectious Disease Research Center, Centre Hospitalier de l'Universite Laval, Quebec City, QC, Can.

SOURCE: Journal of Infectious Diseases (1999), 180(2), 487-490

CODEN: JIDIAQ; ISSN: 0022-1899

PUBLISHER: University of Chicago Press

DOCUMENT TYPE: Journal

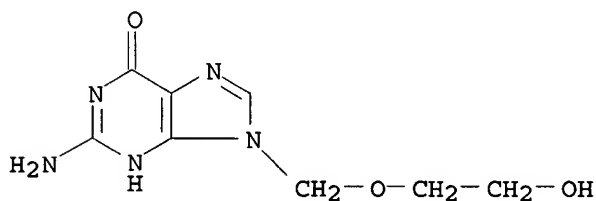
LANGUAGE: English

AB Herpes simplex virus (HSV) isolates were characterized from 8 AIDS patients in whom acyclovir and foscarnet therapy sequentially failed. The 6 postacyclovir (prefoscarnet) HSV isolates were resistant to acyclovir and susceptible to foscarnet. Of the 9

postfoscarnet isolates, 8 were foscarnet-resistant and acyclovir-susceptible, 1 was resistant to both drugs. Acyclovir-resistant isolates retained susceptibility to foscarnet-resistant isolates retained susceptibility to cidofovir. The acyclovir-resistant isolates contained single-base substitutions or frameshift mutations in G or C homopolymer nucleotide repeats of the thymidine kinase gene. In contrast, the foscarnet-resistant strains contained single-base substitutions in conserved (II, III, or VI) or, more rarely, nonconserved (between I and VII) regions of the DNA polymerase (pol) gene. The single isolate exhibiting resistance to acyclovir and foscarnet contained mutations in both genes. In this study of clin. HSV isolates, DNA pol mutations conferring foscarnet resistance were not associated with decreased acyclovir or cidofovir susceptibility.

IT 59277-89-3, Acyclovir
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (phenotypic and genotypic anal. of foscarnet-resistant herpes simplex virus isolates from humans with AIDS resistant to acyclovir and foscarnet)

RN 59277-89-3 HCAPLUS
 CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[(2-hydroxyethoxy)methyl]- (CA INDEX NAME)



REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

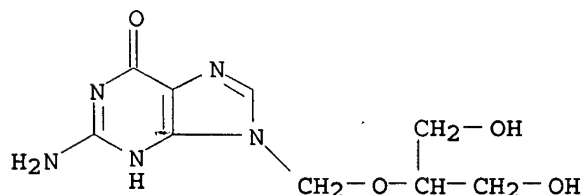
L28 ANSWER 17 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1998:180764 HCAPLUS <<LOGINID::20070502>>
 DOCUMENT NUMBER: 128:248590
 TITLE: Topical antiviral compositions
 INVENTOR(S): Ludwig, John
 PATENT ASSIGNEE(S): Glaxo Group Ltd., UK; Ludwig, John
 SOURCE: PCT Int. Appl., 16 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9810768	A1	19980319	WO 1997-EP4945	19970910 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9743842	A	19980402	AU 1997-43842	19970910 <--

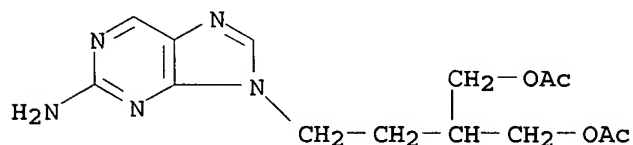
PRIORITY APPLN. INFO.:

GB 1996-18974
WO 1997-EP4945A 19960911
W 19970910

- AB This invention relates to a topical pharmaceutical formulation suitable for use in treating virus infections of the skin and mucosa, and in particular it relates to topical formulations containing compds. having antiviral activity, particularly those active against Herpes Simplex Virus, with the exception of aciclovir. The formulations are oil-in-water topical pharmaceutical formulations comprising a dispersed oil phase and a continuous aqueous phase comprising water, solubilized antiviral compound and at least 10 % of diethylene glycol monoethyl ether. The antiviral compound is selected from penciclovir, famciclovir, ganciclovir, idoxuridine, foscarnet, ribavirin, and cidofovir. The formulations exhibit enhanced efficacy together with low irritancy and good phys. stability. A topical emulsion contained diethylene glycol monoethyl ether (Transcutol) 40, antiviral compound 5, stearyl alc. 5, cetyl alc. 4, light mineral oil 10.2, Brij 721 2.5, Brij 72 2.3, and purified water to 100 %.
- IT 82410-32-0, Ganciclovir 104227-87-4, Famciclovir 113852-37-2, Cidofovir
- RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(topical emulsions containing antiviral compds. and diethylene glycol monoethyl ether)
- RN 82410-32-0 HCAPLUS
- CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[[2-hydroxy-1-(hydroxymethyl)ethoxy]methyl]- (CA INDEX NAME)

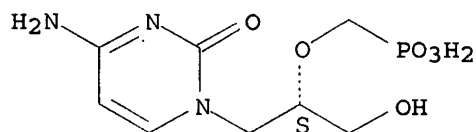


- RN 104227-87-4 HCAPLUS
- CN 1,3-Propanediol, 2-[2-(2-amino-9H-purin-9-yl)ethyl]-, 1,3-diacetate (CA INDEX NAME)



- RN 113852-37-2 HCAPLUS
- CN Phosphonic acid, P-[[[(1S)-2-(4-amino-2-oxo-1(2H)-pyrimidinyl)-1-(hydroxymethyl)ethoxy]methyl]- (CA INDEX NAME)

Absolute stereochemistry.



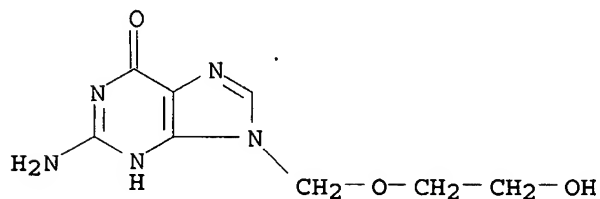
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 18 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1998:121436 HCAPLUS <<LOGINID::20070502>>
 DOCUMENT NUMBER: 128:239028
 TITLE: Successful treatment of an acyclovir- and foscarnet-resistant herpes simplex virus type 1 lesion with intravenous cidofovir
 AUTHOR(S): LoPresti, Antonia E.; Levine, Jerome F.; Munk, Gary B.; Tai, Chun Y.; Mendel, Dirk B.
 CORPORATE SOURCE: Infectious dease Div., Dept. of Internal Medicine and Virology Laboratory, Hackensack University Medical Center, Hackensack, NJ, USA
 SOURCE: Clinical Infectious Diseases (1998), 26(2), 512-513
 CODEN: CIDIEL; ISSN: 1058-4838
 PUBLISHER: University of Chicago Press
 DOCUMENT TYPE: Journal
 LANGUAGE: English

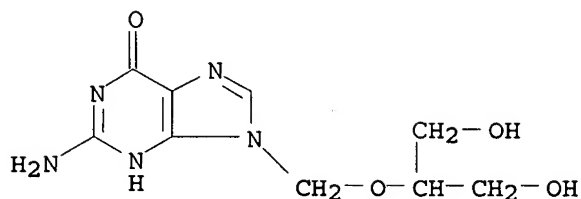
AB This report describes the successful use of i.v. cidofovir to effect rapid and complete resolution of an acyclovir- and foscarnet-resistant HSV-1 lesion in a patient who underwent umbilical cord stem-cell transplantation and who had severe unremitting mucositis of the oropharynx. Treatments with acyclovir, foscarnet and ganciclovir all failed to resolve the mucositis. I.v. cidofovir (5 mg/kg once weekly) with concomitant probenecid therapy was administered, in addition to hydration to reduce the risk of nephrotoxicity. Following three consecutive once-weekly doses of cidofovir, the mucositis cleared. Drug susceptibilities of four HSV isolates obtained from the patient after each antiviral agent revealed increased resistance to acyclovir, foscarnet and ganciclovir following administration of these antivirals. This case suggests potential value of the approved i.v. formulation of cidofovir for the treatment of HSV-1 lesions that are unresponsive to acyclovir and/or foscarnet therapy.

IT 59277-89-3, Acyclovir 82410-32-0, Ganciclovir
 RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (cidofovir treatment of an acyclovir- and foscarnet-resistant herpes simplex virus type 1 lesion in a human)

RN 59277-89-3 HCAPLUS
 CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[(2-hydroxyethoxy)methyl]- (CA INDEX NAME)



RN 82410-32-0 HCAPLUS
 CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[[2-hydroxy-1-(hydroxymethyl)ethoxy]methyl]- (CA INDEX NAME)



IT 113852-37-2, Cidofovir

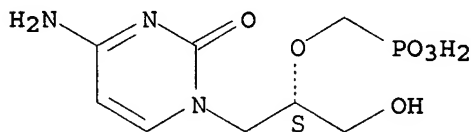
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(cidofovir treatment of an acyclovir- and foscarnet-resistant herpes simplex virus type 1 lesion in a human)

RN 113852-37-2 HCAPLUS

CN Phosphonic acid, P-[[[(1S)-2-(4-amino-2-oxo-1(2H)-pyrimidinyl)-1-(hydroxymethyl)ethoxy]methyl]- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 19 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1997:791030 HCAPLUS <<LOGINID::20070502>>

DOCUMENT NUMBER: 128:86368

TITLE: Antiviral drug susceptibility of human herpesvirus 8

AUTHOR(S): Neyts, Johan; De Clercq, Erik

CORPORATE SOURCE: Rega Institute for Medical Research, Katholieke Universiteit Leuven, Louvain, B-3000, Belg.

SOURCE: Antimicrobial Agents and Chemotherapy (1997), 41(12), 2754-2756

CODEN: AMACQ; ISSN: 0066-4804

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The authors studied the susceptibility of human herpesvirus 8 (HHV-8) to a number of antiherpesvirus agents. The acyclic nucleoside phosphonate (ANP) analogs cidofovir and HPMPA [(S)-1-(3-hydroxy-2-phosphonylmethoxypropyl)adenine] effected potent inhibition of HHV-8 DNA synthesis, with 50% effective concns. (EC50) of 6.3 and 0.6 μ M, resp. Adefovir, an ANP with both antiretrovirus and antiherpesvirus activity, blocked HHV-8 DNA replication at a fourfold-lower concentration than did foscarnet (EC50 of 39 and 177 μ M, resp.). The most potent inhibitory effect was obtained with the N-7-substituted nucleoside analog S2242 (EC50, 0.11 μ M). The nucleoside analogs acyclovir, penciclovir, H2G {(R)-9-[4-hydroxy-2-(hydroxymethyl) butyl]guanine}, and brivudine had weak to moderate effects (EC50 of \geq 75, 43, 42, and 24 μ M, resp., and EC90 of \geq 75 μ M), whereas ganciclovir elicited pronounced anti-HHV-8 activity (EC50, 8.9 μ M).

IT 59277-89-3, Acyclovir 82410-32-0, Ganciclovir

106941-25-7, Adefovir 113852-37-2, Cidofovir

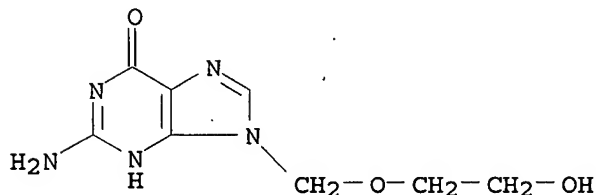
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(antiviral drug susceptibility of human herpesvirus 8)

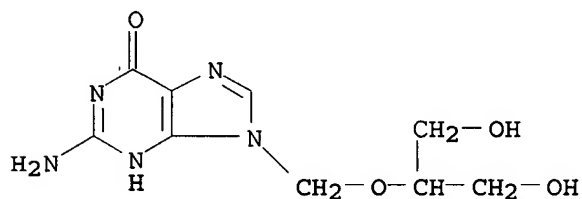
RN 59277-89-3 HCAPLUS

CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[(2-hydroxyethoxy)methyl]- (CA INDEX NAME)



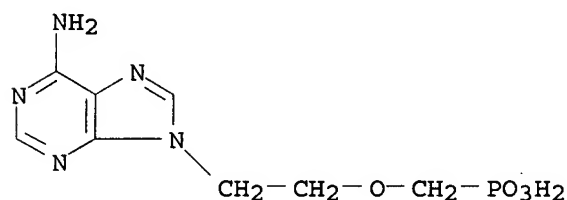
RN 82410-32-0 HCAPLUS

CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[[2-hydroxy-1-(hydroxymethyl)ethoxy]methyl]- (CA INDEX NAME)



RN 106941-25-7 HCAPLUS

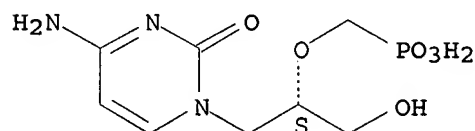
CN Phosphonic acid, P-[[2-(6-amino-9H-purin-9-yl)ethoxy]methyl]- (CA INDEX NAME)



RN 113852-37-2 HCAPLUS

CN Phosphonic acid, P-[[[(1S)-2-(4-amino-2-oxo-1(2H)-pyrimidinyl)-1-(hydroxymethyl)ethoxy]methyl]- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

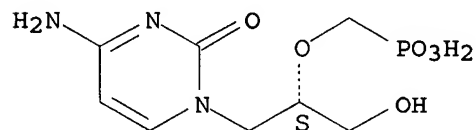
L28 ANSWER 20 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1997:634593 HCAPLUS <<LOGINID::20070502>>
 DOCUMENT NUMBER: 127:287747
 TITLE: Clinical uses of cidofovir
 AUTHOR(S): Safrin, Sharon; Cherrington, Julie; Jaffe, Howard S.
 CORPORATE SOURCE: Gilead Sciences, Foster City, CA, USA
 SOURCE: Reviews in Medical Virology (1997), 7(3),
 145-156
 CODEN: RMVIEW; ISSN: 1052-9276
 PUBLISHER: Wiley
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB Cidofovir is a cytidine nucleotide analog recently licensed as an i.v. treatment for CMV retinitis in AIDS patients. Three controlled clin. trials have demonstrated efficacy of cidofovir for this indication, and have generated data useful as a guideline to prevent potential toxicity. Although de novo emergence of resistance to cidofovir has not been observed clin. in patients receiving cidofovir, cross-resistance to cidofovir in ganciclovir-resistant clin. DNA polymerase mutants has been identified. Cross-resistance of cidofovir and foscarnet has not been identified to date. A broad spectrum agent with in vitro activity against human herpesviruses, adenovirus, HPV, polyomaviruses and human poxviruses, cidofovir is under clin. investigation for a variety of potential applications. Examples include i.v. administration of cidofovir for treatment of progressive multifocal leukoencephalopathy and Kaposi's sarcoma, intraocular injection for treatment of CMV retinitis, intralesional injection for treatment of respiratory papillomatosis, topical application for treatment of molluscum contagiosum, anogenital condyloma acuminata, and recurrent genital herpes, and ophthalmic instillation for treatment of viral keratoconjunctivitis.

IT 113852-37-2, Cidofovir
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (clin. uses of cidofovir in humans)

RN 113852-37-2 HCAPLUS
 CN Phosphonic acid, P-[[[(1S)-2-(4-amino-2-oxo-1(2H)-pyrimidinyl)-1-(hydroxymethyl)ethoxy]methyl]- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 74 THERE ARE 74 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> fil stng

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

121.07

286.71

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE

TOTAL

	ENTRY	SESSION
CA SUBSCRIBER PRICE	-16.38	-31.20

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FILE CONTAINS CURRENT INFORMATION.
 LAST RELOADED: Apr 27, 2007 (20070427/UP).

=> d his

(FILE 'HOME' ENTERED AT 15:58:27 ON 02 MAY 2007)

FILE 'HCAPLUS' ENTERED AT 15:58:36 ON 02 MAY 2007
 E US20040259832/PN 25

L1 1 S E3

FILE 'STNGUIDE' ENTERED AT 15:59:26 ON 02 MAY 2007

FILE 'HCAPLUS' ENTERED AT 16:02:09 ON 02 MAY 2007

L2 43567 S (9002-06-6 OR 4408-78-0 OR 4428-95-9 OR 59277-89-3 OR 66341-
 L3 237600 S (9002-89-5 OR 9004-34-6 OR 9005-25-8 OR 9012-36-6 OR 24980-4
 L4 276194 S L2 OR L3
 L5 1 S L4 AND L1

FILE 'STNGUIDE' ENTERED AT 16:03:41 ON 02 MAY 2007

FILE 'HCAPLUS' ENTERED AT 16:07:58 ON 02 MAY 2007

L6 6746 S (59277-89-3 OR 66341-16-0 OR 82410-32-0 OR 86761-39-9 OR 104
 E HERPES+ALL/CT
 L7 2471 S L6 AND (HERPES OR "HERPES" OR "INFECTION" (L) "HERPES" OR "SK
 L8 113 S ACYCLOVIR ?PHOSPHATE?
 L9 40 S L8 AND L7
 L10 38 S L9 AND 1800<=PY<=2003
 L11 9845 S THYMIDINE KINASE
 L12 24 S L11 AND L10
 L13 76 S THYMIDINE KINASE INHIBITOR
 L14 0 S L13 AND L12
 L15 684 S CIDOFOVIR
 L16 89 S L15 AND L7
 L17 0 S L16 AND L10
 L18 0 S GANCICLOVIR MONOPHOSPHATE
 L19 3504 S GANCICLOVIR
 L20 11 S GANCICLOVIR MONOPHOSPHATE
 L21 2 S L20 AND L7

FILE 'STNGUIDE' ENTERED AT 16:16:23 ON 02 MAY 2007

FILE 'HCAPLUS' ENTERED AT 16:18:06 ON 02 MAY 2007

L22 3 S FORSCARNET
 L23 857 S FORSCARNET
 L24 121 S L23 AND L7
 L25 93 S L24 AND 1800<=PY<=2003

FILE 'STNGUIDE' ENTERED AT 16:19:38 ON 02 MAY 2007

FILE 'HCAPLUS' ENTERED AT 16:20:46 ON 02 MAY 2007

L26 93 S L25 AND (L20 OR L16 OR L13 OR L24 OR L10)
 L27 0 S L25 AND L20
 L28 23 S L25 AND L16
 L29 0 S L25 AND L13

10767019>05/05/2007

L30 93 S L25 AND L24
L31 1 S L25 AND L10

FILE 'STNGUIDE' ENTERED AT 16:23:15 ON 02 MAY 2007

=>

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:ssptarpi1623

PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * Welcome to STN International * * * * *

NEWS 1 Web Page URLs for STN Seminar Schedule - N. America
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NEWS 3 JAN 16 CA/Caplus Company Name Thesaurus enhanced and reloaded
NEWS 4 JAN 16 IPC version 2007.01 thesaurus available on STN
NEWS 5 JAN 16 WPIDS/WPINDEX/WPIX enhanced with IPC 8 reclassification data
NEWS 6 JAN 22 CA/Caplus updated with revised CAS roles
NEWS 7 JAN 22 CA/Caplus enhanced with patent applications from India
NEWS 8 JAN 29 PHAR reloaded with new search and display fields
NEWS 9 JAN 29 CAS Registry Number crossover limit increased to 300,000 in multiple databases
NEWS 10 FEB 15 PATDPASPC enhanced with Drug Approval numbers
NEWS 11 FEB 15 RUSSIAPAT enhanced with pre-1994 records
NEWS 12 FEB 23 KOREAPAT enhanced with IPC 8 features and functionality
NEWS 13 FEB 26 MEDLINE reloaded with enhancements
NEWS 14 FEB 26 EMBASE enhanced with Clinical Trial Number field
NEWS 15 FEB 26 TOXCENTER enhanced with reloaded MEDLINE
NEWS 16 FEB 26 IFICDB/IFIPAT/IFIUDB reloaded with enhancements
NEWS 17 FEB 26 CAS Registry Number crossover limit increased from 10,000 to 300,000 in multiple databases
NEWS 18 MAR 15 WPIDS/WPIX enhanced with new FRAGHITSTR display format
NEWS 19 MAR 16 CASREACT coverage extended
NEWS 20 MAR 20 MARPAT now updated daily
NEWS 21 MAR 22 LWPI reloaded
NEWS 22 MAR 30 RDISCLOSURE reloaded with enhancements
NEWS 23 APR 02 JICST-EPLUS removed from database clusters and STN
NEWS 24 APR 30 GENBANK reloaded and enhanced with Genome Project ID field
NEWS 25 APR 30 CHEMCATS enhanced with 1.2 million new records
NEWS 26 APR 30 CA/Caplus enhanced with 1870-1889 U.S. patent records
NEWS 27 APR 30 INPADOC replaced by INPADOCDB on STN
NEWS 28 MAY 01 New CAS web site launched

NEWS EXPRESS NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.

NEWS HOURS STN Operating Hours Plus Help Desk Availability

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FILE 'HOME' ENTERED AT 11:34:29 ON 03 MAY 2007

=>

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LOGINID:ssptarpil623

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SESSION RESUMED IN FILE 'HOME' AT 11:36:51 ON 03 MAY 2007

FILE 'HOME' ENTERED AT 11:36:51 ON 03 MAY 2007

	SINCE FILE ENTRY	TOTAL SESSION
COST IN U.S. DOLLARS		
FULL ESTIMATED COST	0.21	0.21

=> fil hcaplus

	SINCE FILE ENTRY	TOTAL SESSION
COST IN U.S. DOLLARS		
FULL ESTIMATED COST	0.21	0.21

FILE 'HCAPLUS' ENTERED AT 11:37:07 ON 03 MAY 2007

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=> fil reg

	SINCE FILE ENTRY	TOTAL SESSION
COST IN U.S. DOLLARS		
FULL ESTIMATED COST	2.60	2.81

FILE 'REGISTRY' ENTERED AT 11:37:33 ON 03 MAY 2007

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DICTIONARY FILE UPDATES: 2 MAY 2007 HIGHEST RN 934214-84-3

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on property searching in REGISTRY, refer to:

<http://www.cas.org/support/stngen/stndoc/properties.html>

=> S 161363-19-5/RN
L1 1 161363-19-5/RN

=> FIL CHEMCATS		
COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	0.45	3.26

FILE 'CHEMCATS' ENTERED AT 11:37:59 ON 03 MAY 2007
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prompt. For the list of suppliers currently in the file, enter
HELP SPA, HELP SPBC, HELP SPDH, HELP SPIN, HELP SPOP, and HELP SPQZ.
For the list of current catalogs, enter HELP CTA, HELP CTBC, HELP
CTDH, HELP CTIN, HELP CTOP, and HELP CTQZ.

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=> S L1
L2 0 L1

=> FIL REGISTRY		
COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	0.93	4.19

10767019>05/05/2007

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experimental property data in the original document. For information
on property searching in REGISTRY, refer to:

<http://www.cas.org/support/stngen/stndoc/properties.html>

=> fil hcaplus		
COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	0.45	4.64

FILE 'HCAPLUS' ENTERED AT 11:38:36 ON 03 MAY 2007
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=> s l1
L3 11 L1

=> fil stng		
COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	2.60	7.24

FILE 'STNGUIDE' ENTERED AT 11:38:44 ON 03 MAY 2007
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=> fil hcaplus	SINCE FILE	TOTAL
COST IN U.S. DOLLARS	ENTRY	SESSION
FULL ESTIMATED COST	0.06	7.30

FILE 'HCAPLUS' ENTERED AT 11:39:06 ON 03 MAY 2007
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=> E "161363-19-5"/BI,RN 25

E1	2	161363-18-4/BI
E2	2	161363-18-4P/BI
E3	11 -->	161363-19-5/BI
E4	0	161363-19-5/RN
E5	1	161363-19-5D/BI
E6	3	161363-19-5P/BI
E7	3	161363-20-8/BI
E8	3	161363-20-8P/BI
E9	3	161363-21-9/BI
E10	1	161363-21-9P/BI
E11	1	161363-22-0/BI
E12	1	161363-22-0P/BI
E13	3	161363-23-1/BI
E14	3	161363-23-1P/BI
E15	3	161363-24-2/BI
E16	2	161363-24-2P/BI
E17	3	161363-25-3/BI
E18	1	161363-25-3P/BI
E19	3	161363-26-4/BI
E20	3	161363-26-4P/BI
E21	3	161363-27-5/BI
E22	3	161363-27-5P/BI
E23	1	161363-28-6/BI
E24	1	161363-28-6P/BI
E25	1	161363-29-7/BI

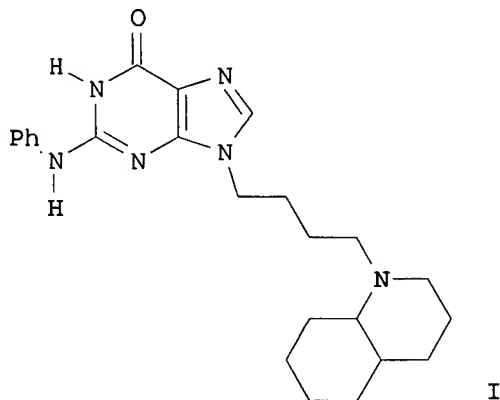
=> S E3 OR E5 OR E6
11 161363-19-5/BI

1 161363-19-5D/BI
 3 161363-19-5P/BI
 L4 11 161363-19-5/BI OR 161363-19-5D/BI OR 161363-19-5P/BI

=> s l4 not l3
 L5 0 L4 NOT L3

=> d l4 ibib abs hitstr

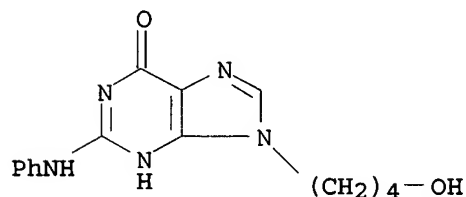
L4 ANSWER 1 OF 11 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2005:398777 HCAPLUS <<LOGINID::20070503>>
 DOCUMENT NUMBER: 143:97319
 TITLE: Inhibition of Herpes Simplex Virus Thymidine Kinases
 by 2-Phenylamino-6-oxopurines and Related Compounds:
 Structure-Activity Relationships and Antiherpetic
 Activity in Vivo
 AUTHOR(S): Manikowski, Andrzej; Verri, Annalisa; Lossani, Andrea;
 Gebhardt, Bryan M.; Gambino, Joseph; Focher, Federico;
 Spadari, Silvio; Wright, George E.
 CORPORATE SOURCE: GLSynthesis Inc., Worcester, MA, 01605, USA
 SOURCE: Journal of Medicinal Chemistry (2005), 48(11),
 3919-3929
 CODEN: JMCMAR; ISSN: 0022-2623
 PUBLISHER: American Chemical Society
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 143:97319
 GI



AB Derivs. of the herpes simplex thymidine kinase inhibitor HBPG [2-phenylamino-9-(4-hydroxybutyl)-6-oxopurine] have been synthesized and tested for inhibitory activity against recombinant enzymes (TK) from herpes simplex types 1 and 2 (HSV-1, HSV-2). The compds. inhibited phosphorylation of [3H]thymidine by both enzymes, but potencies differed quant. from those of HBPG and were generally greater for HSV-2 than HSV-1 TKs. Changes in inhibitory potency were generally consistent with the inhibitor/substrate binding site structure based on published X-ray structures of HSV-1 TK. In particular, several 9-(4-aminobutyl) analogs with bulky tertiary amino substituents were among the most potent inhibitors. Variable substrate assays showed that the most potent compound, 2-phenylamino-9-[4-(1-decahydroquinolinyl)butyl]-6-oxopurine (I·2 HCl), was a competitive inhibitor, with K_i values of 0.03 and 0.005 μM

against HSV-1 and HSV-2 TKs, resp. The parent compound HBPG was uniquely active in viral infection models in mice, both against ocular HSV-2 reactivation and against HSV-1 and HSV-2 encephalitis. In assays lacking [3H]thymidine, HBPG was found to be an efficient substrate for the enzymes. The ability of the TKs to phosphorylate HBPG may relate to its antiherpetic activity in vivo.

IT 161363-19-5
 RL: PAC (Pharmacological activity); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent)
 (inhibition of herpes simplex virus thymidine kinases by 2-phenylamino-6-oxopurines and related compds., structure-activity relationships and antiherpetic activity in vivo)
 RN 161363-19-5 HCAPLUS
 CN 6H-Purin-6-one, 1,9-dihydro-9-(4-hydroxybutyl)-2-(phenylamino)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> fil stng

COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
10.47	17.77

FULL ESTIMATED COST

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SINCE FILE	TOTAL
ENTRY	SESSION
-0.78	-0.78

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=> fil hcaplus

COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
0.24	18.01

FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE	TOTAL
ENTRY	SESSION
0.00	-0.78

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=> E "4408-78-0"/BI,RN 25

E1	1	4408-75-7/BI
E2	2	4408-77-9/BI
E3	648 -->	4408-78-0/BI
E4	0	4408-78-0/RN
E5	47	4408-78-0D/BI
E6	14	4408-78-0DP/BI
E7	45	4408-78-0P/BI
E8	398	4408-81-5/BI
E9	135	4408-81-5D/BI
E10	28	4408-81-5DP/BI
E11	36	4408-81-5P/BI
E12	9	4408-82-6/BI
E13	6	4408-82-6P/BI
E14	3	4408-85-9/BI
E15	1	4408-85-9D/BI
E16	1	4408-86-0/BI
E17	1	4408-92-8/BI
E18	1	4408-92-8P/BI
E19	2	4408-93-9/BI
E20	1	4408-95-1/BI
E21	1	4408-95-1P/BI
E22	71	4408-96-2/BI
E23	69	4408-96-2P/BI
E24	5	4408-97-3/BI
E25	5	4408-97-3P/BI

=> S E3 OR E5 OR E6 OR E7

648	4408-78-0/BI
47	4408-78-0D/BI
14	4408-78-0DP/BI
45	4408-78-0P/BI

L6 648 4408-78-0/BI OR 4408-78-0D/BI OR 4408-78-0DP/BI OR 4408-78-0P/BI

=> E "4428-95-9"/BI,RN 25

E1	11	4428-38-0P/BI
E2	2	4428-39-1/BI
E3	1041 -->	4428-95-9/BI
E4	0	4428-95-9/RN
E5	54	4428-95-9D/BI
E6	11	4428-95-9DP/BI
E7	25	4428-95-9P/BI
E8	63	4428-98-2/BI
E9	8	4428-98-2P/BI
E10	1	44280/BI
E11	2	44280-42-4/BI

E12	2	44280-42-4P/BI
E13	2	44281/BI
E14	1	442816/BI
E15	1	4428178/BI
E16	1	4428229/BI
E17	1	4428246/BI
E18	1	44283/BI
E19	1	442830-09-3/BI
E20	1	4428301/BI
E21	1	4428383/BI
E22	2	44283G/BI
E23	1	44284/BI
E24	1	442842-28-6/BI
E25	1	442842-29-7/BI

=> S E3 OR E5 OR E6 OR E7

1041 4428-95-9/BI
 54 4428-95-9D/BI
 11 4428-95-9DP/BI
 25 4428-95-9P/BI

L7 1041 4428-95-9/BI OR 4428-95-9D/BI OR 4428-95-9DP/BI OR 4428-95-9P/BI

=> E "59277-89-3"/BI,RN 25

E1	3	59277-88-2/BI
E2	3	59277-88-2P/BI
E3	3560 -->	59277-89-3/BI
E4	0	59277-89-3/RN
E5	161	59277-89-3D/BI
E6	74	59277-89-3DP/BI
E7	163	59277-89-3P/BI
E8	4	59277-90-6/BI
E9	3	59277-90-6P/BI
E10	8	59277-91-7/BI
E11	5	59277-91-7P/BI
E12	6	59277-92-8/BI
E13	6	59277-92-8P/BI
E14	4	59277-93-9/BI
E15	4	59277-93-9P/BI
E16	2	59277-94-0/BI
E17	1	59277-94-0P/BI
E18	3	59277-95-1/BI
E19	3	59277-95-1P/BI
E20	5	59277-96-2/BI
E21	3	59277-96-2P/BI
E22	3	59277-97-3/BI
E23	3	59277-97-3P/BI
E24	5	59277-98-4/BI
E25	5	59277-98-4P/BI

=> S E3 OR E5 OR E6 OR E7

3560 59277-89-3/BI
 161 59277-89-3D/BI
 74 59277-89-3DP/BI
 163 59277-89-3P/BI

L8 3560 59277-89-3/BI OR 59277-89-3D/BI OR 59277-89-3DP/BI OR 59277-89-3P/BI

=> E "66341-16-0"/BI,RN 25

E1	5	66341-15-9/BI
E2	3	66341-15-9P/BI
E3	68 -->	66341-16-0/BI
E4	0	66341-16-0/RN
E5	12	66341-16-0D/BI
E6	8	66341-16-0DP/BI

10767019>05/05/2007

E7	26	66341-16-0P/BI
E8	30	66341-17-1/BI
E9	2	66341-17-1D/BI
E10	1	66341-17-1DP/BI
E11	3	66341-17-1P/BI
E12	102	66341-18-2/BI
E13	2	66341-18-2D/BI
E14	7	66341-18-2P/BI
E15	1	66341-19-3/BI
E16	1	66341-19-3P/BI
E17	3	66341-20-6/BI
E18	3	66341-20-6P/BI
E19	1	66341-21-7/BI
E20	1	66341-21-7P/BI
E21	1	66341-22-8/BI
E22	1	66341-22-8P/BI
E23	1	66341-24-0/BI
E24	1	66341-24-0P/BI
E25	1	66341-25-1/BI

=> S E3 OR E5 OR E6 OR E7

68 66341-16-0/BI
12 66341-16-0D/BI
8 66341-16-0DP/BI
26 66341-16-0P/BI

L9 68 66341-16-0/BI OR 66341-16-0D/BI OR 66341-16-0DP/BI OR 66341-16-0P/BI

=> E "82410-32-0"/BI,RN 25

E1	18	82410-31-9/BI
E2	13	82410-31-9P/BI
E3	3177 -->	82410-32-0/BI
E4	0	82410-32-0/RN
E5	81	82410-32-0D/BI
E6	29	82410-32-0DP/BI
E7	80	82410-32-0P/BI
E8	6	82410-33-1/BI
E9	2	82410-33-1P/BI
E10	1	82410-34-2/BI
E11	1	82410-34-2P/BI
E12	7	82410-35-3/BI
E13	2	82410-35-3P/BI
E14	1	82410-36-4/BI
E15	1	82410-36-4P/BI
E16	1	82410-37-5/BI
E17	1	82410-37-5P/BI
E18	1	82410-38-6/BI
E19	1	82410-38-6P/BI
E20	1	82410-39-7/BI
E21	1	82410-39-7P/BI
E22	1	82410-40-0/BI
E23	1	82410-40-0P/BI
E24	1	82410-41-1/BI
E25	1	82410-41-1P/BI

=> S E3 OR E5 OR E6 OR E7

3177 82410-32-0/BI
81 82410-32-0D/BI
29 82410-32-0DP/BI
80 82410-32-0P/BI

L10 3177 82410-32-0/BI OR 82410-32-0D/BI OR 82410-32-0DP/BI OR 82410-32-0P/BI

=> E "86761-39-9"/BI,RN 25

E1	36	86761-38-8/BI
----	----	---------------

E2	3	86761-38-8P/BI
E3	22 -->	86761-39-9/BI
E4	0	86761-39-9/RN
E5	1	86761-39-9D/BI
E6	5	86761-39-9P/BI
E7	1	86761-40-2/BI
E8	1	86761-41-3/BI
E9	1	86761-41-3P/BI
E10	1	86761-42-4/BI
E11	1	86761-42-4P/BI
E12	4	86761-43-5/BI
E13	1	86761-44-6/BI
E14	1	86761-45-7/BI
E15	1	86761-45-7P/BI
E16	1	86761-46-8/BI
E17	1	86761-46-8P/BI
E18	1	86761-47-9/BI
E19	1	86761-47-9P/BI
E20	1	86761-48-0/BI
E21	1	86761-48-0P/BI
E22	1	86761-49-1/BI
E23	1	86761-49-1P/BI
E24	1	86761-50-4/BI
E25	1	86761-50-4P/BI

=> S E3 OR E5 OR E6

22	86761-39-9/BI
1	86761-39-9D/BI
5	86761-39-9P/BI

L11 22 86761-39-9/BI OR 86761-39-9D/BI OR 86761-39-9P/BI

=> E "104227-87-4"/BI,RN 25

E1	34	104227-86-3/BI
E2	17	104227-86-3P/BI
E3	544 -->	104227-87-4/BI
E4	0	104227-87-4/RN
E5	17	104227-87-4D/BI
E6	3	104227-87-4DP/BI
E7	45	104227-87-4P/BI
E8	12	104227-88-5/BI
E9	6	104227-88-5P/BI
E10	8	104227-89-6/BI
E11	8	104227-89-6P/BI
E12	5	104227-90-9/BI
E13	5	104227-90-9P/BI
E14	1	104227-91-0/BI
E15	1	104227-91-0P/BI
E16	1	104227-92-1/BI
E17	1	104227-92-1P/BI
E18	4	104227-93-2/BI
E19	4	104227-93-2P/BI
E20	4	104227-94-3/BI
E21	4	104227-94-3P/BI
E22	4	104227-95-4/BI
E23	4	104227-95-4P/BI
E24	3	104227-96-5/BI
E25	3	104227-96-5P/BI

=> S E3 OR E5 OR E6 OR E7

544	104227-87-4/BI
17	104227-87-4D/BI
3	104227-87-4DP/BI
45	104227-87-4P/BI

10767019>05/05/2007

L12 544 104227-87-4/BI OR 104227-87-4D/BI OR 104227-87-4DP/BI OR 104227-87-4P/BI

=> E "161363-19-5"/BI,RN 25

E1	2	161363-18-4/BI
E2	2	161363-18-4P/BI
E3	11 -->	161363-19-5/BI
E4	0	161363-19-5/RN
E5	1	161363-19-5D/BI
E6	3	161363-19-5P/BI
E7	3	161363-20-8/BI
E8	3	161363-20-8P/BI
E9	3	161363-21-9/BI
E10	1	161363-21-9P/BI
E11	1	161363-22-0/BI
E12	1	161363-22-0P/BI
E13	3	161363-23-1/BI
E14	3	161363-23-1P/BI
E15	3	161363-24-2/BI
E16	2	161363-24-2P/BI
E17	3	161363-25-3/BI
E18	1	161363-25-3P/BI
E19	3	161363-26-4/BI
E20	3	161363-26-4P/BI
E21	3	161363-27-5/BI
E22	3	161363-27-5P/BI
E23	1	161363-28-6/BI
E24	1	161363-28-6P/BI
E25	1	161363-29-7/BI

=> S E3 OR E5 OR E6

11 161363-19-5/BI
1 161363-19-5D/BI
3 161363-19-5P/BI

L13 11 161363-19-5/BI OR 161363-19-5D/BI OR 161363-19-5P/BI

=> E "113852-37-2"/BI,RN 25

E1	9	113852-36-1/BI
E2	4	113852-36-1P/BI
E3	687 -->	113852-37-2/BI
E4	0	113852-37-2/RN
E5	28	113852-37-2D/BI
E6	8	113852-37-2DP/BI
E7	27	113852-37-2P/BI
E8	8	113852-38-3/BI
E9	2	113852-38-3P/BI
E10	3	113852-39-4/BI
E11	1	113852-39-4P/BI
E12	4	113852-40-7/BI
E13	3	113852-40-7P/BI
E14	100	113852-41-8/BI
E15	1	113852-41-8D/BI
E16	9	113852-41-8P/BI
E17	16	113852-42-9/BI
E18	7	113852-42-9P/BI
E19	7	113852-43-0/BI
E20	2	113852-43-0P/BI
E21	3	113852-44-1/BI
E22	1	113852-44-1P/BI
E23	5	113852-46-3/BI
E24	1	113852-46-3P/BI
E25	2	113852-47-4/BI

=> S E3 OR E5 OR E6 OR E7

10767019>05/05/2007

687 113852-37-2/BI
28 113852-37-2D/BI
8 113852-37-2DP/BI
27 113852-37-2P/BI

L14 687 113852-37-2/BI OR 113852-37-2D/BI OR 113852-37-2DP/BI OR 113852-37-2P/BI

=> E "106941-25-7"/BI,RN 25

E1 2 106941-23-5P/BI
E2 1 106941-24-6/BI
E3 648 --> 106941-25-7/BI
E4 0 106941-25-7/RN
E5 27 106941-25-7D/BI
E6 8 106941-25-7DP/BI
E7 42 106941-25-7P/BI
E8 1 106941-26-8/BI
E9 3 106941-27-9/BI
E10 1 106941-28-0/BI
E11 1 106941-28-0P/BI
E12 1 106941-29-1/BI
E13 1 106941-29-1P/BI
E14 1 106941-30-4/BI
E15 1 106941-30-4P/BI
E16 1 106941-31-5/BI
E17 1 106941-31-5P/BI
E18 1 106941-32-6/BI
E19 1 106941-32-6P/BI
E20 4 106941-33-7/BI
E21 3 106941-33-7P/BI
E22 1 106941-34-8/BI
E23 2 106941-35-9/BI
E24 1 106941-35-9P/BI
E25 2 106941-36-0/BI

=> S E3 OR E5 OR E6 OR E7

648 106941-25-7/BI
27 106941-25-7D/BI
8 106941-25-7DP/BI
42 106941-25-7P/BI

L15 648 106941-25-7/BI OR 106941-25-7D/BI OR 106941-25-7DP/BI OR 106941-25-7P/BI

=> d his

(FILE 'HOME' ENTERED AT 11:34:29 ON 03 MAY 2007)

FILE 'HCAPLUS' ENTERED AT 11:37:07 ON 03 MAY 2007

FILE 'REGISTRY' ENTERED AT 11:37:33 ON 03 MAY 2007

L1 1 S 161363-19-5/RN

FILE 'CHEMCATS' ENTERED AT 11:37:59 ON 03 MAY 2007

SET LIN 80

L2 0 S L1

FILE 'REGISTRY' ENTERED AT 11:38:09 ON 03 MAY 2007

FILE 'HCAPLUS' ENTERED AT 11:38:36 ON 03 MAY 2007

L3 11 S L1

FILE 'STNGUIDE' ENTERED AT 11:38:44 ON 03 MAY 2007

FILE 'HCAPLUS' ENTERED AT 11:39:06 ON 03 MAY 2007

E "161363-19-5"/BI,RN 25

L4 11 S E3 OR E5 OR E6

L5 0 S L4 NOT L3

FILE 'STNGUIDE' ENTERED AT 11:40:03 ON 03 MAY 2007

FILE 'HCAPLUS' ENTERED AT 11:42:16 ON 03 MAY 2007

E "4408-78-0"/BI,RN 25
 L6 648 S E3 OR E5 OR E6 OR E7
 E "4428-95-9"/BI,RN 25
 L7 1041 S E3 OR E5 OR E6 OR E7
 E "59277-89-3"/BI,RN 25
 L8 3560 S E3 OR E5 OR E6 OR E7
 E "66341-16-0"/BI,RN 25
 L9 68 S E3 OR E5 OR E6 OR E7
 E "82410-32-0"/BI,RN 25
 L10 3177 S E3 OR E5 OR E6 OR E7
 E "86761-39-9"/BI,RN 25
 L11 22 S E3 OR E5 OR E6
 E "104227-87-4"/BI,RN 25
 L12 544 S E3 OR E5 OR E6 OR E7
 E "161363-19-5"/BI,RN 25
 L13 11 S E3 OR E5 OR E6
 E "113852-37-2"/BI,RN 25
 L14 687 S E3 OR E5 OR E6 OR E7
 E "106941-25-7"/BI,RN 25
 L15 648 S E3 OR E5 OR E6 OR E7

=> s l4 and l6

L16 1 L4 AND L6

=> d l16 ibib abs hitstr

L16 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:681513 HCAPLUS <<LOGINID::20070503>>

DOCUMENT NUMBER: 141:185078

TITLE: Novel antiherpes drug combinations of Herpes simplex virus thymidine kinase inhibitors and antiherpes substances

INVENTOR(S): Wright, George E.

PATENT ASSIGNEE(S): University of Massachusetts, USA

SOURCE: PCT Int. Appl., 22 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004069168	A2	20040819	WO 2004-US2427	20040129
WO 2004069168	A3	20050915		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2514334	A1	20040819	CA 2004-2514334	20040129
US 2004259832	A1	20041223	US 2004-767019	20040129
EP 1594507	A2	20051116	EP 2004-706459	20040129
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				

PRIORITY APPLN. INFO.:

US 2003-443519P

P 20030129

WO 2004-US2427

W 20040129

AB Composition and methods are disclosed that include a synergistic combination of an inhibitor of Herpes simplex virus thymidine kinase, and an antiherpes substance. The effect of combination of 2-phenylamino-9-(4-hydroxybutyl)-6-oxopurine and foscarnet against HSV2 encephalitis in mice was examined

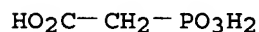
IT 4408-78-0 161363-19-5

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(antiherpes drug combinations of Herpes simplex virus thymidine kinase inhibitors and antiherpes substances)

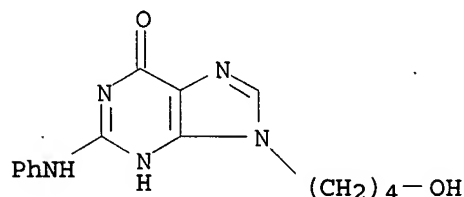
RN 4408-78-0 HCAPLUS

CN Acetic acid, 2-phosphono- (CA INDEX NAME)



RN 161363-19-5 HCAPLUS

CN 6H-Purin-6-one, 1,9-dihydro-9-(4-hydroxybutyl)-2-(phenylamino)- (9CI) (CA INDEX NAME)



=> d his

(FILE 'HOME' ENTERED AT 11:34:29 ON 03 MAY 2007)

FILE 'HCAPLUS' ENTERED AT 11:37:07 ON 03 MAY 2007

FILE 'REGISTRY' ENTERED AT 11:37:33 ON 03 MAY 2007

L1 1 S 161363-19-5/RN

FILE 'CHEMCATS' ENTERED AT 11:37:59 ON 03 MAY 2007

SET LIN 80

L2 0 S L1

FILE 'REGISTRY' ENTERED AT 11:38:09 ON 03 MAY 2007

FILE 'HCAPLUS' ENTERED AT 11:38:36 ON 03 MAY 2007

L3 11 S L1

FILE 'STNGUIDE' ENTERED AT 11:38:44 ON 03 MAY 2007

FILE 'HCAPLUS' ENTERED AT 11:39:06 ON 03 MAY 2007

E "161363-19-5"/BI,RN 25

L4 11 S E3 OR E5 OR E6

L5 0 S L4 NOT L3

FILE 'STNGUIDE' ENTERED AT 11:40:03 ON 03 MAY 2007

FILE 'HCAPLUS' ENTERED AT 11:42:16 ON 03 MAY 2007

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L6      648 S E3 OR E5 OR E6 OR E7
          E "4408-78-0"/BI,RN 25
L7      1041 S E3 OR E5 OR E6 OR E7
          E "4428-95-9"/BI,RN 25
L8      3560 S E3 OR E5 OR E6 OR E7
          E "59277-89-3"/BI,RN 25
L9      68 S E3 OR E5 OR E6 OR E7
          E "66341-16-0"/BI,RN 25
L10     3177 S E3 OR E5 OR E6 OR E7
          E "82410-32-0"/BI,RN 25
L11     22 S E3 OR E5 OR E6
          E "86761-39-9"/BI,RN 25
L12     544 S E3 OR E5 OR E6 OR E7
          E "104227-87-4"/BI,RN 25
L13     11 S E3 OR E5 OR E6
          E "161363-19-5"/BI,RN 25
L14     687 S E3 OR E5 OR E6 OR E7
          E "113852-37-2"/BI,RN 25
L15     648 S E3 OR E5 OR E6 OR E7
          E "106941-25-7"/BI,RN 25
L16     1 S L4 AND L6

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=> s l4 and l7

L17 1 L4 AND L7

=> s l4 and l8

L18 5 L4 AND L8

=> s l17 not l16

L19 0 L17 NOT L16

=> s l18 not l16

L20 4 L18 NOT L16

=> d l20 ibib abs hitstr 1-4

L20 ANSWER 1 OF 4 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:398777 HCAPLUS <<LOGINID::20070503>>

DOCUMENT NUMBER: 143:97319

TITLE: Inhibition of Herpes Simplex Virus Thymidine Kinases
by 2-Phenylamino-6-oxopurines and Related Compounds:
Structure-Activity Relationships and Antiherpetic
Activity in Vivo

AUTHOR(S): Manikowski, Andrzej; Verri, Annalisa; Lossani, Andrea;
Gebhardt, Bryan M.; Gambino, Joseph; Focher, Federico;
Spadari, Silvio; Wright, George E.

CORPORATE SOURCE: GLSynthesis Inc., Worcester, MA, 01605, USA
SOURCE: Journal of Medicinal Chemistry (2005), 48(11),
3919-3929

CODEN: JMCMAR; ISSN: 0022-2623

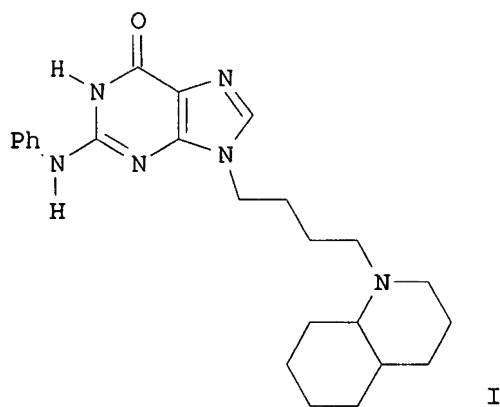
PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 143:97319

GI

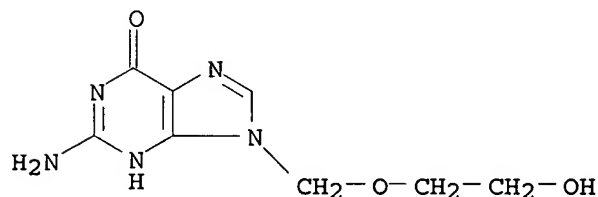


AB Derivs. of the herpes simplex thymidine kinase inhibitor HBPG [2-phenylamino-9-(4-hydroxybutyl)-6-oxopurine] have been synthesized and tested for inhibitory activity against recombinant enzymes (TK) from herpes simplex types 1 and 2 (HSV-1, HSV-2). The compds. inhibited phosphorylation of [3H]thymidine by both enzymes, but potencies differed quant. from those of HBPG and were generally greater for HSV-2 than HSV-1 TKs. Changes in inhibitory potency were generally consistent with the inhibitor/substrate binding site structure based on published X-ray structures of HSV-1 TK. In particular, several 9-(4-aminobutyl) analogs with bulky tertiary amino substituents were among the most potent inhibitors. Variable substrate assays showed that the most potent compound, 2-phenylamino-9-[4-(1-decahydroquinolyl)butyl]-6-oxopurine (I·2 HCl), was a competitive inhibitor, with K_i values of 0.03 and 0.005 μM against HSV-1 and HSV-2 TKs, resp. The parent compound HBPG was uniquely active in viral infection models in mice, both against ocular HSV-2 reactivation and against HSV-1 and HSV-2 encephalitis. In assays lacking [3H]thymidine, HBPG was found to be an efficient substrate for the enzymes. The ability of the TKs to phosphorylate HBPG may relate to its antiherpetic activity in vivo.

IT 59277-89-3, Acyclovir
 RL: PAC (Pharmacological activity); BIOL (Biological study)
 (inhibition of herpes simplex virus thymidine kinases by
 2-phenylamino-6-oxopurines and related compds., structure-activity
 relationships and antiherpetic activity in vivo)

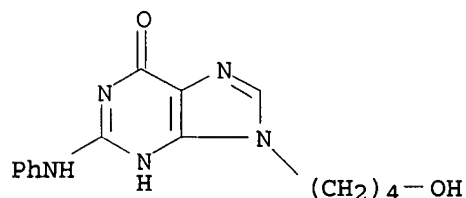
RN 59277-89-3 HCAPLUS

CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[(2-hydroxyethoxy)methyl]- (CA
 INDEX NAME)



IT 161363-19-5
 RL: PAC (Pharmacological activity); RCT (Reactant); BIOL (Biological
 study); RACT (Reactant or reagent)
 (inhibition of herpes simplex virus thymidine kinases by
 2-phenylamino-6-oxopurines and related compds., structure-activity
 relationships and antiherpetic activity in vivo)

RN 161363-19-5 HCAPLUS
 CN 6H-Purin-6-one, 1,9-dihydro-9-(4-hydroxybutyl)-2-(phenylamino)- (9CI) (CA
 INDEX NAME)



REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:134376 HCAPLUS <<LOGINID::20070503>>

DOCUMENT NUMBER: 142:366752

TITLE: Binding Mode Prediction of Cytochrome P450 and
 Thymidine Kinase Protein-Ligand Complexes by
 Consideration of Water and Rescoring in Automated
 Docking

AUTHOR(S): de Graaf, Chris; Pospisil, Pavel; Pos, Wouter;
 Folkers, Gerd; Vermeulen, Nico P. E.

CORPORATE SOURCE: Leiden/Amsterdam Center for Drug Research, Division of
 Molecular Toxicology, Vrije Universiteit Amsterdam,
 Amsterdam, 1081 HV, Neth.

SOURCE: Journal of Medicinal Chemistry (2005), 48(7),
 2308-2318

CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The popular docking programs AutoDock, FlexX, and GOLD were used to
 predict binding modes of ligands in crystallog. complexes including x-ray
 water mols. or computationally predicted water mols. Isoenzymes of two
 different enzyme systems were used, namely cytochromes P 450 (n = 19) and
 thymidine kinases (n = 19) and three different "water" scenarios: i.e.,
 docking (i) into water-free active sites, (ii) into active sites containing
 crystallog. water mols., and (iii) into active sites containing water mols.
 predicted by a novel approach based on the program GRID. Docking
 accuracies were determined in terms of the root-mean-square deviation (RMSD)
 accuracy and, newly defined, in terms of the ligand catalytic site
 prediction (CSP) accuracy. Consideration of both x-ray and predicted
 water mols. and the subsequent pooling and rescoring of all solns.
 (generated by all three docking programs) with the SCORE scoring function
 significantly improved the quality of prediction of the binding modes both
 in terms of RMSD and CSP accuracy.

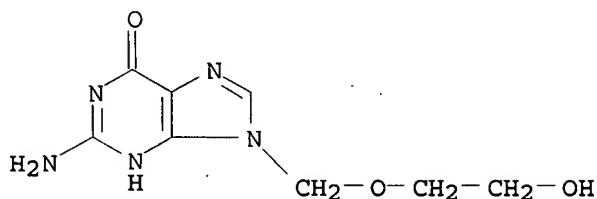
IT 59277-89-3, Acyclovir 161363-19-5

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)

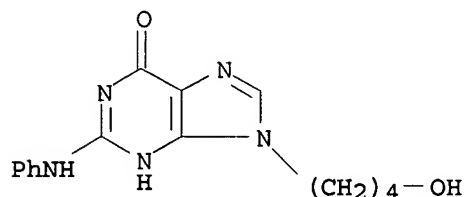
(binding mode prediction of cytochrome P 450 and thymidine kinase
 protein-ligand complexes by consideration of water and rescoring in
 automated docking)

RN 59277-89-3 HCAPLUS

CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[(2-hydroxyethoxy)methyl]- (CA
 INDEX NAME)



RN 161363-19-5 HCAPLUS
 CN 6H-Purin-6-one, 1,9-dihydro-9-(4-hydroxybutyl)-2-(phenylamino)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:457254 HCAPLUS <<LOGINID::20070503>>

DOCUMENT NUMBER: 135:207324

TITLE: The rational of catalytic activity of herpes simplex virus thymidine kinase. A combined biochemical and quantum chemical study

AUTHOR(S): Sulpizi, Marialore; Schelling, Pierre; Folkers, Gerd; Carloni, Paolo; Scapozza, Leonardo

CORPORATE SOURCE: International School Advanced Studies, Scuola Internazionale Superiore Studi Aranzati, Trieste, 34013, Italy

SOURCE: Journal of Biological Chemistry (2001), 276(24), 21692-21697

CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Most antiherpes therapies exploit the large substrate acceptance of herpes simplex virus type 1 thymidine kinase (TK HSV1) relative to the human isoenzyme. The enzyme selectively phosphorophorylates nucleoside analogs that can either inhibit viral DNA polymerase or cause toxic effects when incorporated into viral DNA. To relate structural properties of TKHSV1 ligands to their chemical reactivity we have carried out ab initio quantum chemical calcns. withing the d. functional theory framework in combination with biochem. studies. Calcns. have focused on a set of ligands carrying a representative set of the large spectrum of sugar-mimicking moieties and for which structural information of the TKHSV1ligand complex is available. The kcat values of these ligands have been measured under the same exptl. conditions using an UV spectrophotometric assay. The calcns. point to the crucial role of elec. dipole moment of ligands and its interaction with the neg. charged residue Glu225. A striking correlation is found between the energetics associated with this interaction and the kcat values measured under homogeneous conditions. This finding uncovers a fundamental aspect of the mechanism governing substrate diversity and

catalytic turnover and thus represents a significant step toward the rational design of novel and powerful prodrugs for antiviral and TKHSV1-linked suicide gene therapies.

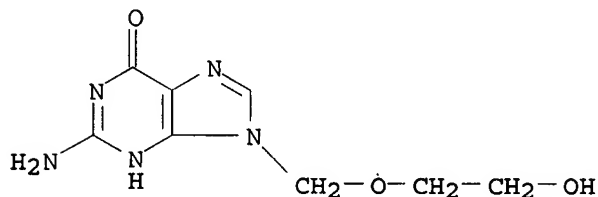
IT 59277-89-3, Aciclovir 161363-19-5

RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)

(biochem. and quantum chemical study of nucleoside analogs interaction with herpes simplex virus thymidine kinase)

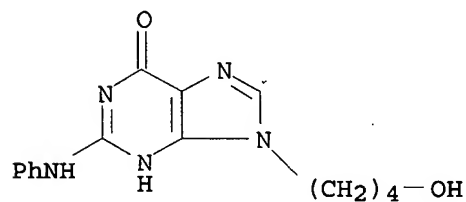
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CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[(2-hydroxyethoxy)methyl]- (CA INDEX NAME)



RN 161363-19-5 HCAPLUS

CN 6H-Purin-6-one, 1,9-dihydro-9-(4-hydroxybutyl)-2-(phenylamino)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:60517 HCAPLUS <<LOGINID::20070503>>

DOCUMENT NUMBER: 130:293191

TITLE: Structure to 1.9 Å resolution of a complex with herpes simplex virus type-1 thymidine kinase of a novel, non-substrate inhibitor: X-ray crystallographic comparison with binding of aciclovir

AUTHOR(S): Bennett, Matthew S.; Wien, Frank; Champness, John N.; Batuwangala, Thilina; Rutherford, Thomas; Summers, William C.; Sun, Hongmao; Wright, George; Sanderson, Mark R.

CORPORATE SOURCE: Randall Institute, Division of Biomedical Sciences, King's College, London, WC2B 5RL, UK

SOURCE: FEBS Letters (1999), 443(2), 121-125
CODEN: FEBLAL; ISSN: 0014-5793

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Treatment of herpes infections with nucleoside analogs requires as an initial step the activation of the compds. by thymidine kinase. As an aid to developing more effective chemotherapy, both for treatment of recurrent herpes infection and in gene therapy systems where thymidine kinase is

expressed, two high-resolution X-ray structures of thymidine kinase have been compared: one with the relatively poor substrate aciclovir (Zovirax), the other with a synthetic inhibitor having an N2-substituted guanine (HBPG; 9-(4-hydroxybutyl)-N2-phenylguanine). Both compds. have similar binding modes in spite of their size difference and apparently distinct ligand properties.

IT 59277-89-3D, Aciclovir, thymidine kinase complexes

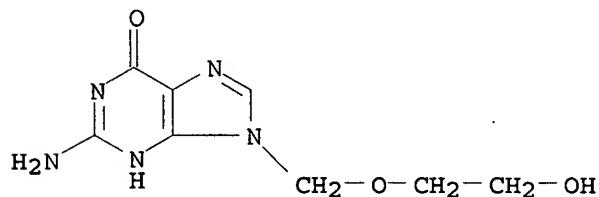
161363-19-5D, thymidine kinase complexes

RL: PRP (Properties)

(crystal structure to 1.9 Å resolution of a complex with herpes simplex virus type-1 thymidine kinase of a novel, non-substrate inhibitor and comparison with binding of aciclovir)

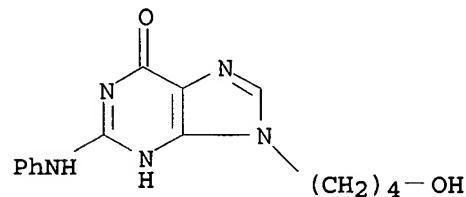
RN 59277-89-3 HCAPLUS

CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[(2-hydroxyethoxy)methyl]- (CA INDEX NAME)



RN 161363-19-5 HCAPLUS

CN 6H-Purin-6-one, 1,9-dihydro-9-(4-hydroxybutyl)-2-(phenylamino)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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FILE 'HCAPLUS' ENTERED AT 11:37:07 ON 03 MAY 2007

FILE 'REGISTRY' ENTERED AT 11:37:33 ON 03 MAY 2007

L1 1 S 161363-19-5/RN

FILE 'CHEMCATS' ENTERED AT 11:37:59 ON 03 MAY 2007

SET LIN 80

L2 0 S L1

FILE 'REGISTRY' ENTERED AT 11:38:09 ON 03 MAY 2007

FILE 'HCAPLUS' ENTERED AT 11:38:36 ON 03 MAY 2007

L3 11 S L1

FILE 'STNGUIDE' ENTERED AT 11:38:44 ON 03 MAY 2007

FILE 'HCAPLUS' ENTERED AT 11:39:06 ON 03 MAY 2007

E "161363-19-5"/BI,RN 25

L4 11 S E3 OR E5 OR E6

L5 0 S L4 NOT L3

FILE 'STNGUIDE' ENTERED AT 11:40:03 ON 03 MAY 2007

FILE 'HCAPLUS' ENTERED AT 11:42:16 ON 03 MAY 2007

E "4408-78-0"/BI,RN 25

L6 648 S E3 OR E5 OR E6 OR E7

E "4428-95-9"/BI,RN 25

L7 1041 S E3 OR E5 OR E6 OR E7

E "59277-89-3"/BI,RN 25

L8 3560 S E3 OR E5 OR E6 OR E7

E "66341-16-0"/BI,RN 25

L9 68 S E3 OR E5 OR E6 OR E7

E "82410-32-0"/BI,RN 25

L10 3177 S E3 OR E5 OR E6 OR E7

E "86761-39-9"/BI,RN 25

L11 22 S E3 OR E5 OR E6

E "104227-87-4"/BI,RN 25

L12 544 S E3 OR E5 OR E6 OR E7

E "161363-19-5"/BI,RN 25

L13 11 S E3 OR E5 OR E6

E "113852-37-2"/BI,RN 25

L14 687 S E3 OR E5 OR E6 OR E7

E "106941-25-7"/BI,RN 25

L15 648 S E3 OR E5 OR E6 OR E7

L16 1 S L4 AND L6

L17 1 S L4 AND L7

L18 5 S L4 AND L8

L19 0 S L17 NOT L16

L20 4 S L18 NOT L16

=> s l4 and l9

L21 1 L4 AND L9

=> s l21 not l16

L22 0 L21 NOT L16

=> s l4 and l10

L23 3 L4 AND L10

=> s l23 not l16

L24 2 L23 NOT L16

=> d l24 ibib abs hitstr 1-2

L24 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:134376 HCAPLUS <<LOGINID::20070503>>

DOCUMENT NUMBER: 142:366752

TITLE: Binding Mode Prediction of Cytochrome P450 and
Thymidine Kinase Protein-Ligand Complexes by
Consideration of Water and Rescoring in Automated
Docking

AUTHOR(S): de Graaf, Chris; Pospisil, Pavel; Pos, Wouter;
Folkers, Gerd; Vermeulen, Nico P. E.

CORPORATE SOURCE: Leiden/Amsterdam Center for Drug Research, Division of
Molecular Toxicology, Vrije Universiteit Amsterdam,
Amsterdam, 1081 HV, Neth.

SOURCE: Journal of Medicinal Chemistry (2005), 48(7),
2308-2318
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The popular docking programs AutoDock, FlexX, and GOLD were used to predict binding modes of ligands in crystallog. complexes including x-ray water mols. or computationally predicted water mols. Isoenzymes of two different enzyme systems were used, namely cytochromes P 450 (n = 19) and thymidine kinases (n = 19) and three different "water" scenarios: i.e., docking (i) into water-free active sites, (ii) into active sites containing crystallog. water mols., and (iii) into active sites containing water mols. predicted by a novel approach based on the program GRID. Docking accuracies were determined in terms of the root-mean-square deviation (RMSD) accuracy and, newly defined, in terms of the ligand catalytic site prediction (CSP) accuracy. Consideration of both x-ray and predicted water mols. and the subsequent pooling and rescoring of all solns. (generated by all three docking programs) with the SCORE scoring function significantly improved the quality of prediction of the binding modes both in terms of RMSD and CSP accuracy.

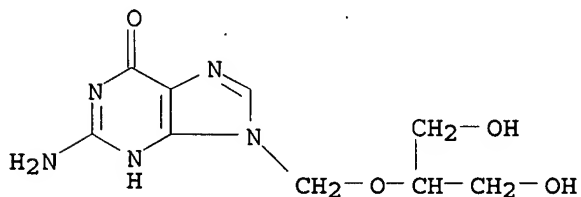
IT 82410-32-0, Ganciclovir 161363-19-5

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(binding mode prediction of cytochrome P 450 and thymidine kinase protein-ligand complexes by consideration of water and rescoring in automated docking)

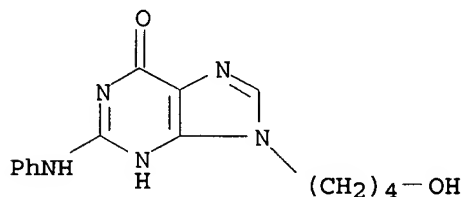
RN 82410-32-0 HCAPLUS

CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[[2-hydroxy-1-(hydroxymethyl)ethoxy]methyl]- (CA INDEX NAME)



RN 161363-19-5 HCAPLUS

CN 6H-Purin-6-one, 1,9-dihydro-9-(4-hydroxybutyl)-2-(phenylamino)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:457254 HCAPLUS <<LOGINID::20070503>>

DOCUMENT NUMBER: 135:207324

TITLE: The rational of catalytic activity of herpes simplex virus thymidine kinase. A combined biochemical and quantum chemical study

AUTHOR(S): Sulpizi, Marialore; Schelling, Pierre; Folkers, Gerd; Carloni, Paolo; Scapozza, Leonardo

CORPORATE SOURCE: International School Advanced Studies, Scuola Internazionale Superiore Studi Aranzati, Trieste, 34013, Italy

SOURCE: Journal of Biological Chemistry (2001), 276(24), 21692-21697
CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal

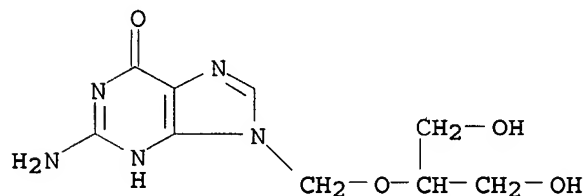
LANGUAGE: English

AB Most antiherpes therapies exploit the large substrate acceptance of herpes simplex virus type 1 thymidine kinase (TK HSV1) relative to the human isoenzyme. The enzyme selectively phosphorophorylates nucleoside analogs that can either inhibit viral DNA polymerase or cause toxic effects when incorporated into viral DNA. To relate structural properties of TKHSV1 ligands to their chemical reactivity we have carried out ab initio quantum chemical calcns. withing the d. functional theory framework in combination with biochem. studies. Calcns. have focused on a set of ligands carrying a representative set of the large spectrum of sugar-mimicking moieties and for which structural information of the TKHSV1ligand complex is available. The kcat values of these ligands have been measured under the same exptl. conditions using an UV spectrophotometric assay. The calcns. point to the crucial role of elec. dipole moment of ligands and its interaction with the neg. charged residue Glu225. A striking correlation is found between the energetics associated with this interaction and the kcat values measured under homogeneous conditions. This finding uncovers a fundamental aspect of the mechanism governing substrate diversity and catalytic turnover and thus represents a significant step toward the rational design of novel and powerful prodrugs for antiviral and TKHSV1-linked suicide gene therapies.

IT 82410-32-0, Ganciclovir 161363-19-5
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(biochem. and quantum chemical study of nucleoside analogs interaction with herpes simplex virus thymidine kinase)

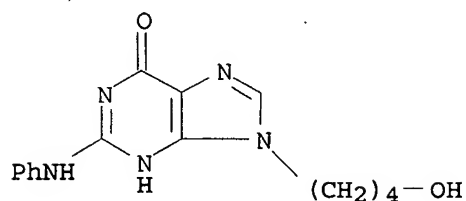
RN 82410-32-0 HCAPLUS

CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[[2-hydroxy-1-(hydroxymethyl)ethoxy)methyl]- (CA INDEX NAME)



RN 161363-19-5 HCAPLUS

CN 6H-Purin-6-one, 1,9-dihydro-9-(4-hydroxybutyl)-2-(phenylamino)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d his

(FILE 'HOME' ENTERED AT 11:34:29 ON 03 MAY 2007)

FILE 'HCAPLUS' ENTERED AT 11:37:07 ON 03 MAY 2007

FILE 'REGISTRY' ENTERED AT 11:37:33 ON 03 MAY 2007
L1 1 S 161363-19-5/RN

FILE 'CHEMCATS' ENTERED AT 11:37:59 ON 03 MAY 2007
SET LIN 80
L2 0 S L1

FILE 'REGISTRY' ENTERED AT 11:38:09 ON 03 MAY 2007

FILE 'HCAPLUS' ENTERED AT 11:38:36 ON 03 MAY 2007
L3 11 S L1

FILE 'STNGUIDE' ENTERED AT 11:38:44 ON 03 MAY 2007

FILE 'HCAPLUS' ENTERED AT 11:39:06 ON 03 MAY 2007
E "161363-19-5"/BI,RN 25
L4 11 S E3 OR E5 OR E6
L5 0 S L4 NOT L3

FILE 'STNGUIDE' ENTERED AT 11:40:03 ON 03 MAY 2007

FILE 'HCAPLUS' ENTERED AT 11:42:16 ON 03 MAY 2007
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L6 648 S E3 OR E5 OR E6 OR E7
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L7 1041 S E3 OR E5 OR E6 OR E7
E "59277-89-3"/BI,RN 25
L8 3560 S E3 OR E5 OR E6 OR E7
E "66341-16-0"/BI,RN 25
L9 68 S E3 OR E5 OR E6 OR E7
E "82410-32-0"/BI,RN 25
L10 3177 S E3 OR E5 OR E6 OR E7
E "86761-39-9"/BI,RN 25
L11 22 S E3 OR E5 OR E6
E "104227-87-4"/BI,RN 25
L12 544 S E3 OR E5 OR E6 OR E7
E "161363-19-5"/BI,RN 25
L13 11 S E3 OR E5 OR E6
E "113852-37-2"/BI,RN 25
L14 687 S E3 OR E5 OR E6 OR E7
E "106941-25-7"/BI,RN 25
L15 648 S E3 OR E5 OR E6 OR E7
L16 1 S L4 AND L6

L17 1 S L4 AND L7
 L18 5 S L4 AND L8
 L19 0 S L17 NOT L16
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L28 0 L27 NOT L16

=> s l4 and l14

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=> s l4 and l15

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=> s (l29 or l30) not l16

L31 0 (L29 OR L30) NOT L16

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LAST RELOADED: Apr 27, 2007 (20070427/UP).

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FILE CONTAINS CURRENT INFORMATION.

LAST RELOADED: Apr 27, 2007 (20070427/UP).

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 NEWS 3 JAN 16 CA/Caplus Company Name Thesaurus enhanced and reloaded
 NEWS 4 JAN 16 IPC version 2007.01 thesaurus available on STN
 NEWS 5 JAN 16 WPIDS/WPINDEX/WPIX enhanced with IPC 8 reclassification data
 NEWS 6 JAN 22 CA/Caplus updated with revised CAS roles
 NEWS 7 JAN 22 CA/Caplus enhanced with patent applications from India
 NEWS 8 JAN 29 PHAR reloaded with new search and display fields
 NEWS 9 JAN 29 CAS Registry Number crossover limit increased to 300,000 in multiple databases
 NEWS 10 FEB 15 PATDPASPC enhanced with Drug Approval numbers
 NEWS 11 FEB 15 RUSSIAPAT enhanced with pre-1994 records
 NEWS 12 FEB 23 KOREAPAT enhanced with IPC 8 features and functionality
 NEWS 13 FEB 26 MEDLINE reloaded with enhancements
 NEWS 14 FEB 26 EMBASE enhanced with Clinical Trial Number field
 NEWS 15 FEB 26 TOXCENTER enhanced with reloaded MEDLINE
 NEWS 16 FEB 26 IFICDB/IFIPAT/IFIUDB reloaded with enhancements
 NEWS 17 FEB 26 CAS Registry Number crossover limit increased from 10,000 to 300,000 in multiple databases
 NEWS 18 MAR 15 WPIDS/WPIX enhanced with new FRAGHITSTR display format
 NEWS 19 MAR 16 CASREACT coverage extended
 NEWS 20 MAR 20 MARPAT now updated daily
 NEWS 21 MAR 22 LWPI reloaded
 NEWS 22 MAR 30 RDISCLOSURE reloaded with enhancements
 NEWS 23 APR 02 JICST-EPLUS removed from database clusters and STN
 NEWS 24 APR 30 GENBANK reloaded and enhanced with Genome Project ID field
 NEWS 25 APR 30 CHEMCATS enhanced with 1.2 million new records
 NEWS 26 APR 30 CA/Caplus enhanced with 1870-1889 U.S. patent records
 NEWS 27 APR 30 INPADOC replaced by INPADOCDB on STN
 NEWS 28 MAY 01 New CAS web site launched
 NEWS EXPRESS NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.
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FILE COVERS 1907 - 3 May 2007 VOL ISS

FILE LAST UPDATED: 2 May 2007 (20070502/ED)

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E15	1	104227-91-0P/BI
E16	1	104227-92-1/BI
E17	1	104227-92-1P/BI
E18	4	104227-93-2/BI
E19	4	104227-93-2P/BI
E20	4	104227-94-3/BI
E21	4	104227-94-3P/BI
E22	4	104227-95-4/BI
E23	4	104227-95-4P/BI
E24	3	104227-96-5/BI
E25	3	104227-96-5P/BI

=> S E3 OR E5 OR E6 OR E7

544	104227-87-4/BI
17	104227-87-4D/BI
3	104227-87-4DP/BI
45	104227-87-4P/BI

L2 544 104227-87-4/BI OR 104227-87-4D/BI OR 104227-87-4DP/BI OR 104227-87-4P/BI

=> E "161363-19-5"/BI,RN 25

E1	2	161363-18-4/BI
E2	2	161363-18-4P/BI
E3	11 -->	161363-19-5/BI
E4	0	161363-19-5/RN
E5	1	161363-19-5D/BI
E6	3	161363-19-5P/BI
E7	3	161363-20-8/BI
E8	3	161363-20-8P/BI
E9	3	161363-21-9/BI
E10	1	161363-21-9P/BI
E11	1	161363-22-0/BI
E12	1	161363-22-0P/BI
E13	3	161363-23-1/BI
E14	3	161363-23-1P/BI
E15	3	161363-24-2/BI
E16	2	161363-24-2P/BI
E17	3	161363-25-3/BI
E18	1	161363-25-3P/BI
E19	3	161363-26-4/BI
E20	3	161363-26-4P/BI
E21	3	161363-27-5/BI
E22	3	161363-27-5P/BI
E23	1	161363-28-6/BI
E24	1	161363-28-6P/BI
E25	1	161363-29-7/BI

=> S E3 OR E5 OR E6

11 161363-19-5/BI
1 161363-19-5D/BI
3 161363-19-5P/BI

L3 11 161363-19-5/BI OR 161363-19-5D/BI OR 161363-19-5P/BI

=> E "113852-37-2"/BI,RN 25

E1	9	113852-36-1/BI
E2	4	113852-36-1P/BI
E3	687 -->	113852-37-2/BI
E4	0	113852-37-2/RN
E5	28	113852-37-2D/BI
E6	8	113852-37-2DP/BI
E7	27	113852-37-2P/BI
E8	8	113852-38-3/BI
E9	2	113852-38-3P/BI
E10	3	113852-39-4/BI
E11	1	113852-39-4P/BI
E12	4	113852-40-7/BI
E13	3	113852-40-7P/BI
E14	100	113852-41-8/BI
E15	1	113852-41-8D/BI
E16	9	113852-41-8P/BI
E17	16	113852-42-9/BI
E18	7	113852-42-9P/BI
E19	7	113852-43-0/BI
E20	2	113852-43-0P/BI
E21	3	113852-44-1/BI
E22	1	113852-44-1P/BI
E23	5	113852-46-3/BI
E24	1	113852-46-3P/BI
E25	2	113852-47-4/BI

=> S E3 OR E5 OR E6 OR E7

687 113852-37-2/BI
 28 113852-37-2D/BI
 8 113852-37-2DP/BI
 27 113852-37-2P/BI

L4 687 113852-37-2/BI OR 113852-37-2D/BI OR 113852-37-2DP/BI OR 113852-37-2P/BI

=> E "106941-25-7"/BI,RN 25

E1 2 106941-23-5P/BI
 E2 1 106941-24-6/BI
 E3 648 --> 106941-25-7/BI
 E4 0 106941-25-7/RN
 E5 27 106941-25-7D/BI
 E6 8 106941-25-7DP/BI
 E7 42 106941-25-7P/BI
 E8 1 106941-26-8/BI
 E9 3 106941-27-9/BI
 E10 1 106941-28-0/BI
 E11 1 106941-28-0P/BI
 E12 1 106941-29-1/BI
 E13 1 106941-29-1P/BI
 E14 1 106941-30-4/BI
 E15 1 106941-30-4P/BI
 E16 1 106941-31-5/BI
 E17 1 106941-31-5P/BI
 E18 1 106941-32-6/BI
 E19 1 106941-32-6P/BI
 E20 4 106941-33-7/BI
 E21 3 106941-33-7P/BI
 E22 1 106941-34-8/BI
 E23 2 106941-35-9/BI
 E24 1 106941-35-9P/BI
 E25 2 106941-36-0/BI

=> S E3 OR E5 OR E6 OR E7

648 106941-25-7/BI
 27 106941-25-7D/BI
 8 106941-25-7DP/BI
 42 106941-25-7P/BI

L5 648 106941-25-7/BI OR 106941-25-7D/BI OR 106941-25-7DP/BI OR 106941-25-7P/BI

=> his

HIS IS NOT A RECOGNIZED COMMAND

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 "HELP COMMANDS" at an arrow prompt (=>).

=> d his

(FILE 'HOME' ENTERED AT 14:27:11 ON 03 MAY 2007)

FILE 'HCAPLUS' ENTERED AT 14:27:17 ON 03 MAY 2007

E "86761-39-9"/BI,RN 25
 L1 22 S E3 OR E5 OR E6
 E "104227-87-4"/BI,RN 25
 E "104227-87-4"/BI,RN 25
 L2 544 S E3 OR E5 OR E6 OR E7
 E "161363-19-5"/BI,RN 25
 L3 11 S E3 OR E5 OR E6
 E "113852-37-2"/BI,RN 25
 L4 687 S E3 OR E5 OR E6 OR E7
 E "106941-25-7"/BI,RN 25
 L5 648 S E3 OR E5 OR E6 OR E7

10767019>05/05/2007

=> s l1-l5

L6 1634 (L1 OR L2 OR L3 OR L4 OR L5)

=> s l3 and (l1 or l2 or l4 or l5)

L7 1 L3 AND (L1 OR L2 OR L4 OR L5)

=> d ti

L7 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2007 ACS on STN

TI Novel antiherpes drug combinations of Herpes simplex virus thymidine kinase inhibitors and antiherpes substances

=> fil stng

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

10.74

10.95

FILE 'STNGUIDE' ENTERED AT 14:29:43 ON 03 MAY 2007

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LAST RELOADED: Apr 27, 2007 (20070427/UP).

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LOGOFF? (Y)/N/HOLD:y

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

0.06

11.01

STN INTERNATIONAL LOGOFF AT 14:30:11 ON 03 MAY 2007

Connecting via Winsock to STN

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PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

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NEWS 3 JAN 16 CA/CAPlus Company Name Thesaurus enhanced and reloaded
NEWS 4 JAN 16 IPC version 2007.01 thesaurus available on STN
NEWS 5 JAN 16 WPIDS/WPINDEX/WPIX enhanced with IPC 8 reclassification data
NEWS 6 JAN 22 CA/CAPlus updated with revised CAS roles
NEWS 7 JAN 22 CA/CAPlus enhanced with patent applications from India
NEWS 8 JAN 29 PHAR reloaded with new search and display fields
NEWS 9 JAN 29 CAS Registry Number crossover limit increased to 300,000 in multiple databases
NEWS 10 FEB 15 PATDPASPC enhanced with Drug Approval numbers

NEWS 11 FEB 15 RUSSIAPAT enhanced with pre-1994 records
 NEWS 12 FEB 23 KOREAPAT enhanced with IPC 8 features and functionality
 NEWS 13 FEB 26 MEDLINE reloaded with enhancements
 NEWS 14 FEB 26 EMBASE enhanced with Clinical Trial Number field
 NEWS 15 FEB 26 TOXCENTER enhanced with reloaded MEDLINE
 NEWS 16 FEB 26 IFICDB/IFIPAT/IFIUDB reloaded with enhancements
 NEWS 17 FEB 26 CAS Registry Number crossover limit increased from 10,000
 to 300,000 in multiple databases
 NEWS 18 MAR 15 WPIDS/WPIX enhanced with new FRAGHITSTR display format
 NEWS 19 MAR 16 CASREACT coverage extended
 NEWS 20 MAR 20 MARPAT now updated daily
 NEWS 21 MAR 22 LWPI reloaded
 NEWS 22 MAR 30 RDISCLOSURE reloaded with enhancements
 NEWS 23 APR 02 JICST-EPLUS removed from database clusters and STN
 NEWS 24 APR 30 GENBANK reloaded and enhanced with Genome Project ID field
 NEWS 25 APR 30 CHEMCATS enhanced with 1.2 million new records
 NEWS 26 APR 30 CA/Caplus enhanced with 1870-1889 U.S. patent records
 NEWS 27 APR 30 INPADOC replaced by INPADOCDB on STN
 NEWS 28 MAY 01 New CAS web site launched

NEWS EXPRESS NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT
 MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
 AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.

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=> fil hcaplus		
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	ENTRY	SESSION
FULL ESTIMATED COST	0.21	0.21

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FILE COVERS 1907 - 3 May 2007 VOL 146 ISS 19

FILE LAST UPDATED: 1 May 2007 (20070501/ED)

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This file contains CAS Registry Numbers for easy and accurate

=> E WRIGHT G/AU 25

E1	1	WRIGHT FRITZ M/AU
E2	3	WRIGHT FULTON JR/AU
E3	76 -->	WRIGHT G/AU
E4	53	WRIGHT G A/AU
E5	4	WRIGHT G A E/AU
E6	1	WRIGHT G ALBERT/AU
E7	13	WRIGHT G B/AU
E8	8	WRIGHT G C/AU
E9	9	WRIGHT G D/AU
E10	1	WRIGHT G D S/AU
E11	17	WRIGHT G E/AU
E12	21	WRIGHT G F/AU
E13	3	WRIGHT G F JR/AU
E14	6	WRIGHT G G/AU
E15	1	WRIGHT G G H/AU
E16	7	WRIGHT G H/AU
E17	43	WRIGHT G J/AU
E18	54	WRIGHT G L/AU
E19	9	WRIGHT G L JR/AU
E20	17	WRIGHT G M/AU
E21	3	WRIGHT G MCN/AU
E22	1	WRIGHT G N/AU
E23	7	WRIGHT G P/AU
E24	31	WRIGHT G PAYLING/AU
E25	11	WRIGHT G R/AU

=> E 25

E26	1	WRIGHT G R G/AU
E27	30	WRIGHT G S/AU
E28	31	WRIGHT G T/AU
E29	20	WRIGHT G W/AU
E30	1	WRIGHT G WAYNE/AU
E31	2	WRIGHT G Z/AU
E32	6	WRIGHT GABRIELA/AU
E33	1	WRIGHT GABRIELA M/AU
E34	1	WRIGHT GABRIELA M J S/AU
E35	2	WRIGHT GABRIELLA/AU
E36	5	WRIGHT GAIL C/AU
E37	1	WRIGHT GAIL E/AU
E38	1	WRIGHT GAIL K/AU
E39	2	WRIGHT GAIL P/AU
E40	1	WRIGHT GAIL SHAW/AU
E41	5	WRIGHT GARCIA KIMBERLEY/AU
E42	2	WRIGHT GARDNER V/AU
E43	17	WRIGHT GARY/AU
E44	10	WRIGHT GARY A/AU
E45	1	WRIGHT GARY ALAN/AU
E46	1	WRIGHT GARY B/AU
E47	2	WRIGHT GARY C/AU
E48	1	WRIGHT GARY D/AU
E49	1	WRIGHT GARY J/AU
E50	3	WRIGHT GARY JOHN/AU

=> E 25

E51	22	WRIGHT GARY L/AU
E52	1	WRIGHT GARY LEE/AU

E53	1	WRIGHT GARY LESLIE/AU
E54	20	WRIGHT GAVIN/AU
E55	10	WRIGHT GAVIN J/AU
E56	1	WRIGHT GENE A/AU
E57	6	WRIGHT GENESIS P/AU
E58	1	WRIGHT GEO/AU
E59	4	WRIGHT GEO C/AU
E60	53	WRIGHT GEO F/AU
E61	8	WRIGHT GEO G/AU
E62	1	WRIGHT GEO G JR/AU
E63	1	WRIGHT GEO H/AU
E64	1	WRIGHT GEO J/AU
E65	2	WRIGHT GEO M/AU
E66	1	WRIGHT GEO T/AU
E67	5	WRIGHT GEO W/AU
E68	3	WRIGHT GEOFF/AU
E69	1	WRIGHT GEOFF C/AU
E70	1	WRIGHT GEOFF R/AU
E71	3	WRIGHT GEOFFREY/AU
E72	1	WRIGHT GEOFFREY A/AU
E73	1	WRIGHT GEOFFREY ANTHONY/AU
E74	1	WRIGHT GEOFFREY B/AU
E75	4	WRIGHT GEOFFREY R/AU

=> E 25

E76	1	WRIGHT GEOFFRY R/AU
E77	46	WRIGHT GEORGE/AU
E78	2	WRIGHT GEORGE A/AU
E79	81	WRIGHT GEORGE B/AU
E80	7	WRIGHT GEORGE BUFORD/AU
E81	57	WRIGHT GEORGE C/AU
E82	3	WRIGHT GEORGE C JR/AU
E83	4	WRIGHT GEORGE CARLIN/AU
E84	1	WRIGHT GEORGE D/AU
E85	105	WRIGHT GEORGE E/AU
E86	4	WRIGHT GEORGE EDWARD/AU
E87	150	WRIGHT GEORGE F/AU
E88	1	WRIGHT GEORGE F JR/AU
E89	15	WRIGHT GEORGE G/AU
E90	2	WRIGHT GEORGE GREEN/AU
E91	1	WRIGHT GEORGE H/AU
E92	4	WRIGHT GEORGE HENRY/AU
E93	1	WRIGHT GEORGE HODGSON/AU
E94	22	WRIGHT GEORGE J/AU
E95	5	WRIGHT GEORGE JOSEPH/AU
E96	5	WRIGHT GEORGE L/AU
E97	65	WRIGHT GEORGE L JR/AU
E98	3	WRIGHT GEORGE LEONARD JR/AU
E99	5	WRIGHT GEORGE M/AU
E100	1	WRIGHT GEORGE MARTIN/AU

=> E 25

E101	4	WRIGHT GEORGE T/AU
E102	1	WRIGHT GEORGE TODD/AU
E103	13	WRIGHT GEORGE W/AU
E104	2	WRIGHT GEORGE WAYNE/AU
E105	1	WRIGHT GEORGE WILBUR/AU
E106	1	WRIGHT GEORGE WILLIAM/AU
E107	3	WRIGHT GEORGES/AU
E108	2	WRIGHT GEORGIA E/AU
E109	3	WRIGHT GERALD D/AU
E110	2	WRIGHT GERALDINE/AU
E111	10	WRIGHT GERALDINE A/AU

E112	4	WRIGHT GERARD/AU
E113	91	WRIGHT GERARD D/AU
E114	2	WRIGHT GERRY/AU
E115	1	WRIGHT GILES/AU
E116	5	WRIGHT GILLIAN/AU
E117	11	WRIGHT GILLIAN S/AU
E118	1	WRIGHT GLEN LAWRENCE/AU
E119	36	WRIGHT GLENDA M/AU
E120	1	WRIGHT GLENDA MARY/AU
E121	3	WRIGHT GLENFORD/AU
E122	1	WRIGHT GLENN A/AU
E123	7	WRIGHT GLENN C/AU
E124	1	WRIGHT GLENN E/AU
E125	1	WRIGHT GLENN T/AU

=> E WRIGHT GEORGE/AU 25

E1	4	WRIGHT GEOFFREY R/AU
E2	1	WRIGHT GEOFFRY R/AU
E3	46 -->	WRIGHT GEORGE/AU
E4	2	WRIGHT GEORGE A/AU
E5	81	WRIGHT GEORGE B/AU
E6	7	WRIGHT GEORGE BUFORD/AU
E7	57	WRIGHT GEORGE C/AU
E8	3	WRIGHT GEORGE C JR/AU
E9	4	WRIGHT GEORGE CARLIN/AU
E10	1	WRIGHT GEORGE D/AU
E11	105	WRIGHT GEORGE E/AU
E12	4	WRIGHT GEORGE EDWARD/AU
E13	150	WRIGHT GEORGE F/AU
E14	1	WRIGHT GEORGE F JR/AU
E15	15	WRIGHT GEORGE G/AU
E16	2	WRIGHT GEORGE GREEN/AU
E17	1	WRIGHT GEORGE H/AU
E18	4	WRIGHT GEORGE HENRY/AU
E19	1	WRIGHT GEORGE HODGSON/AU
E20	22	WRIGHT GEORGE J/AU
E21	5	WRIGHT GEORGE JOSEPH/AU
E22	5	WRIGHT GEORGE L/AU
E23	65	WRIGHT GEORGE L JR/AU
E24	3	WRIGHT GEORGE LEONARD JR/AU
E25	5	WRIGHT GEORGE M/AU

=> S (E3 OR E4 OR E5 OR E6 OR E7 OR E8 OR E9 OR E10 OR E11 OR E12 OR E13 OR E14 OR E15 OR E16 OR E17 OR E18 OR E19 OR E20 OR E21 OR E22 OR E23 OR E24 OR E25)

46	"WRIGHT GEORGE"/AU
2	"WRIGHT GEORGE A"/AU
81	"WRIGHT GEORGE B"/AU
7	"WRIGHT GEORGE BUFORD"/AU
57	"WRIGHT GEORGE C"/AU
3	"WRIGHT GEORGE C JR"/AU
4	"WRIGHT GEORGE CARLIN"/AU
1	"WRIGHT GEORGE D"/AU
105	"WRIGHT GEORGE E"/AU
4	"WRIGHT GEORGE EDWARD"/AU
150	"WRIGHT GEORGE F"/AU
1	"WRIGHT GEORGE F JR"/AU
15	"WRIGHT GEORGE G"/AU
2	"WRIGHT GEORGE GREEN"/AU
1	"WRIGHT GEORGE H"/AU
4	"WRIGHT GEORGE HENRY"/AU
1	"WRIGHT GEORGE HODGSON"/AU
22	"WRIGHT GEORGE J"/AU
5	"WRIGHT GEORGE JOSEPH"/AU

5 "WRIGHT GEORGE L"/AU
 65 "WRIGHT GEORGE L JR"/AU
 3 "WRIGHT GEORGE LEONARD JR"/AU
 5 "WRIGHT GEORGE M"/AU
 L1 588 ("WRIGHT GEORGE"/AU OR "WRIGHT GEORGE A"/AU OR "WRIGHT GEORGE B"/AU OR "WRIGHT
 GEORGE BUFORD"/AU OR "WRIGHT GEORGE C"/AU OR "WRIGHT GEORGE C JR"/AU OR "WRIGHT GEORGE
 CARLIN"/AU OR "WRIGHT GEORGE D"/AU OR "WRIGHT GEORGE E"/AU OR "WRIGH
 T GEORGE EDWARD"/AU OR "WRIGHT GEORGE F"/AU OR "WRIGHT GEORGE F JR"/AU OR
 "WRIGHT GEORGE G"/AU OR "WRIGHT GEORGE GREEN"/AU OR "WRIGHT GEORGE H"/AU OR "WRIGHT GEORGE
 HENRY"/AU OR "WRIGHT GEORGE HODGSON"/AU OR "WRIGHT GEORGE J"/AU OR
 "WRIGHT GEORGE JOSEPH"/AU OR "WRIGHT GEORGE L"/AU OR "WRIGHT GEORGE L JR"/AU OR
 "WRIGHT GEORGE LEONARD JR"/AU OR "WRIGHT GEORGE M"/AU)

=> E 25

E26	1	WRIGHT GEORGE MARTIN/AU
E27	4	WRIGHT GEORGE T/AU
E28	1	WRIGHT GEORGE TODD/AU
E29	13	WRIGHT GEORGE W/AU
E30	2	WRIGHT GEORGE WAYNE/AU
E31	1	WRIGHT GEORGE WILBUR/AU
E32	1	WRIGHT GEORGE WILLIAM/AU
E33	3	WRIGHT GEORGES/AU
E34	2	WRIGHT GEORGIA E/AU
E35	3	WRIGHT GERALD D/AU
E36	2	WRIGHT GERALDINE/AU
E37	10	WRIGHT GERALDINE A/AU
E38	4	WRIGHT GERARD/AU
E39	91	WRIGHT GERARD D/AU
E40	2	WRIGHT GERRY/AU
E41	1	WRIGHT GILES/AU
E42	5	WRIGHT GILLIAN/AU
E43	11	WRIGHT GILLIAN S/AU
E44	1	WRIGHT GLEN LAWRENCE/AU
E45	36	WRIGHT GLENDA M/AU
E46	1	WRIGHT GLENDA MARY/AU
E47	3	WRIGHT GLENFORD/AU
E48	1	WRIGHT GLENN A/AU
E49	7	WRIGHT GLENN C/AU
E50	1	WRIGHT GLENN E/AU

=> S (E26 OR E27 OR E28 OR E29 OR E30 OR E31 OR E32)

1 "WRIGHT GEORGE MARTIN"/AU
 4 "WRIGHT GEORGE T"/AU
 1 "WRIGHT GEORGE TODD"/AU
 13 "WRIGHT GEORGE W"/AU
 2 "WRIGHT GEORGE WAYNE"/AU
 1 "WRIGHT GEORGE WILBUR"/AU
 1 "WRIGHT GEORGE WILLIAM"/AU
 L2 23 ("WRIGHT GEORGE MARTIN"/AU OR "WRIGHT GEORGE T"/AU OR "WRIGHT GEORGE TODD"/AU
 OR "WRIGHT GEORGE W"/AU OR "WRIGHT GEORGE WAYNE"/AU OR "WRIGHT GEORGE WILBUR"/AU OR "WRIGHT
 GEORGE WILLIAM"/AU)

=> s 11 or 12

L3 611 L1 OR L2

=> s 13 and herpes

26188 HERPES

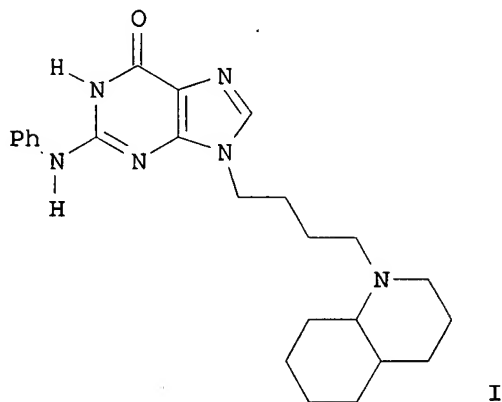
L4 19 L3 AND HERPES

=> d 14 ibib abs

L4 ANSWER 1 OF 19 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:398777 HCAPLUS <<LOGINID::20070503>>

DOCUMENT NUMBER: 143:97319
 TITLE: Inhibition of Herpes Simplex Virus Thymidine Kinases by 2-Phenylamino-6-oxopurines and Related Compounds: Structure-Activity Relationships and Antiherpetic Activity in Vivo
 AUTHOR(S): Manikowski, Andrzej; Verri, Annalisa; Lossani, Andrea; Gebhardt, Bryan M.; Gambino, Joseph; Focher, Federico; Spadari, Silvio; Wright, George E.
 CORPORATE SOURCE: GLSynthesis Inc., Worcester, MA, 01605, USA
 SOURCE: Journal of Medicinal Chemistry (2005), 48(11), 3919-3929
 CODEN: JMCMAR; ISSN: 0022-2623
 PUBLISHER: American Chemical Society
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 143:97319
 GI



AB Derivs. of the herpes simplex thymidine kinase inhibitor HBPG [2-phenylamino-9-(4-hydroxybutyl)-6-oxopurine] have been synthesized and tested for inhibitory activity against recombinant enzymes (TK) from herpes simplex types 1 and 2 (HSV-1, HSV-2). The compds. inhibited phosphorylation of [3H]thymidine by both enzymes, but potencies differed quant. from those of HBPG and were generally greater for HSV-2 than HSV-1 TKs. Changes in inhibitory potency were generally consistent with the inhibitor/substrate binding site structure based on published X-ray structures of HSV-1 TK. In particular, several 9-(4-aminobutyl) analogs with bulky tertiary amino substituents were among the most potent inhibitors. Variable substrate assays showed that the most potent compound, 2-phenylamino-9-[4-(1-decahydroquinolyl)butyl]-6-oxopurine (I·2 HCl), was a competitive inhibitor, with K_i values of 0.03 and 0.005 μM against HSV-1 and HSV-2 TKs, resp. The parent compound HBPG was uniquely active in viral infection models in mice, both against ocular HSV-2 reactivation and against HSV-1 and HSV-2 encephalitis. In assays lacking [3H]thymidine, HBPG was found to be an efficient substrate for the enzymes. The ability of the TKs to phosphorylate HBPG may relate to its antiherpetic activity in vivo.

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> s 14 and combinat?

617320 COMBINAT?

L5 1 L4 AND COMBINAT?

=> d ti

L5 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2007 ACS on STN

TI Novel antiherpes drug combinations of Herpes simplex
virus thymidine kinase inhibitors and antiherpes substances

=> d l4 ibib abs 2-5

L4 ANSWER 2 OF 19 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:681513 HCAPLUS <<LOGINID::20070503>>

DOCUMENT NUMBER: 141:185078

TITLE: Novel antiherpes drug combinations of Herpes
simplex virus thymidine kinase inhibitors and
antiherpes substances

INVENTOR(S): Wright, George E.

PATENT ASSIGNEE(S): University of Massachusetts, USA

SOURCE: PCT Int. Appl., 22 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004069168	A2	20040819	WO 2004-US2427	20040129
WO 2004069168	A3	20050915		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2514334	A1	20040819	CA 2004-2514334	20040129
US 2004259832	A1	20041223	US 2004-767019	20040129
EP 1594507	A2	20051116	EP 2004-706459	20040129
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
PRIORITY APPLN. INFO.:			US 2003-443519P	P 20030129
			WO 2004-US2427	W 20040129

AB Composition and methods are disclosed that include a synergistic combination of an inhibitor of Herpes simplex virus thymidine kinase, and an antiherpes substance. The effect of combination of 2-phenylamino-9-(4-hydroxybutyl)-6-oxopurine and foscarnet against HSV2 encephalitis in mice was examined

L4 ANSWER 3 OF 19 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:58588 HCAPLUS <<LOGINID::20070503>>

DOCUMENT NUMBER: 134:115965

TITLE: Preparation of uracil derivatives as inhibitors of
Herpes simplex virus uracil-DNA glycosylase

INVENTOR(S): Wright, George E.

PATENT ASSIGNEE(S): University of Massachusetts Medical Center, USA

SOURCE: U.S., 19 pp.

CODEN: USXXAM

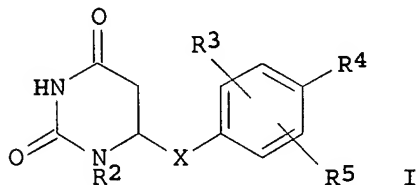
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6177437	B1	20010123	US 1999-388006	19990901
PRIORITY APPLN. INFO.:			US 1998-99274P	P 19980904
OTHER SOURCE(S):	MARPAT 134:115965			
GI				



AB 6-Aromatic substituted uracil compds. I [X = O, NR₁, CH₂ and R₁ = H, alkyl; R₂ = H, alkyl, = (un)substituted Ph, alkoxyalkyl, etc.; R₃, R₅ = H, carboxamido, etc.; R₄ = alkyl, alkenyl, alkoxy] were prepared Methods of treating Herpes simplex virus Type I and Type II recurrent infections and Herpes simplex virus Type I and Type II encephalitis in humans using the compds. and/or therapeutic compns. are investigated. E.g., a mixture of 6-chlorouracil and 4-decylaniline was heated to 200° to give 90% 6-(4-decylanilino)uracil.

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 19 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2000:34133 HCAPLUS <<LOGINID::20070503>>

DOCUMENT NUMBER: 132:302785

TITLE: Status of inhibitors of herpes simplex thymidine kinases

AUTHOR(S): Wright, George E.; Gambino, Joseph J.; Sun, Hongmao; Gebhardt, Bryan M.

CORPORATE SOURCE: GL Synthesis Inc, Shrewsbury, MA, 01545, USA

SOURCE: Current Opinion in Anti-Infective Investigational Drugs (1999), 1(5), 541-546
CODEN: COADFY; ISSN: 1464-8458

PUBLISHER: Current Drugs Ltd.

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review with 23 refs. Determination of the crystal structures of complexes of herpes simplex virus type 1 thymidine kinase (HSV1 TK) with its substrates has provided a detailed picture of the active site and an understanding of the wide substrate range of the enzyme. The binding mode of a class of nonsubstrate inhibitors, exemplified by 9-(4-hydroxybutyl)-N²-phenylguanine (HBPG), has been revealed in the crystal structure of the TK:HBPG complex, allowing rational design of improved inhibitors. Further studies of the effect of HBPG in a murine model of HSV1 latency demonstrated the promise of TK inhibitors in preventing reactivation of herpetic diseases.

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 19 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:371578 HCAPLUS <<LOGINID::20070503>>

DOCUMENT NUMBER: 131:164978

TITLE: Molecular Modeling and Synthesis of Inhibitors of Herpes Simplex Virus Type 1 Uracil-DNA Glycosylase

AUTHOR(S): Sun, Hongmao; Zhi, Chengxin; Wright, George E.; Ubiali, Daniela; Pregnolato, Massimo; Verri, Annalisa; Focher, Federico; Spadari, Silvio

CORPORATE SOURCE: Department of Pharmacology and Molecular Toxicology, University of Massachusetts Medical Center, Worcester, MA, 01655, USA

SOURCE: Journal of Medicinal Chemistry (1999), 42(13), 2344-2350
CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Properties of the first selective inhibitors of herpes simplex virus type 1 (HSV1) uracil-DNA glycosylase (UDG), an enzyme of DNA repair that has been proposed to be required for reactivation of the virus from latency, have been reported recently. 6-(4-Octylanilino)uracil (octAU) was the most potent inhibitor among a series of 6-(4-alkylanilino)uracils, acting in the micromolar range and without effect against human UDG. A 28.5-kDa catalytic fragment of HSV1 UDG has been crystallized in the presence of uracil, and the structure was recently solved. The coordinates of this structure were used in order to study interaction of inhibitors with the enzyme, and a model of binding between octAU and UDG was derived. Starting with the optimized model, the activity of several octAU analogs was predicted, and the values compared favorably with exptl. results found for the synthetic compds. Several hydrophilic derivs. were predicted and found to be active as UDG inhibitors. These compds. will be useful to determine if UDG, like the viral thymidine kinase, is required for reactivation of HSV1 from latency in nerve cells.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> fil stng

COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
30.09	30.30

FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE	TOTAL
ENTRY	SESSION
-3.90	-3.90

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FILE CONTAINS CURRENT INFORMATION.

LAST RELOADED: Apr 27, 2007 (20070427/UP).

=> fil hcaplus

COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
0.06	30.36

FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE	TOTAL
ENTRY	SESSION
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FILE 'HCAPLUS' ENTERED AT 15:08:55 ON 03 MAY 2007

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FILE COVERS 1907 - 3 May 2007 VOL ISS
 FILE LAST UPDATED: 2 May 2007 (20070502/ED)
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FILE COVERS 1907 - 3 May 2007 VOL 146 ISS 19
 FILE LAST UPDATED: 1 May 2007 (20070501/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate

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    278677 "INFECTION"
    80500 "INFECTIONS"
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    9533 "INFECTION" (L) "HERPES"
    255396 "SKIN"
    10347 "SKINS"
    261265 "SKIN"
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    950309 "DISEASE"
    257327 "DISEASES"
    1065511 "DISEASE"
        ("DISEASE" OR "DISEASES")
    32845 "SKIN, DISEASE"
        ("SKIN" (W) "DISEASE")
    26188 "HERPES"
    490 "SKIN, DISEASE" (L) "HERPES"
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    504026 COMBINATION
    116308 COMBINATIONS
    594825 COMBINATION
        (COMBINATION OR COMBINATIONS)
    312210 THERAPY
    28032 THERAPIES
    327271 THERAPY
        (THERAPY OR THERAPIES)
    11979 COMBINATION THERAPY
        (COMBINATION (W) THERAPY)
    38843 "E1"
    5595846 "0"
    9117716 "1"
    504026 "COMBINATION"
    116308 "COMBINATIONS"
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27808 "CT"
1385 "CTS"
28972 "CT"
      ("CT" OR "CTS")
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312210 "THERAPY"
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327271 "THERAPY"
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6390 "E4"
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28972 "CT"
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277 "3888"
1912220 "9"
22619 "COMBINATORIAL"
5 "COMBINATORIALS"
22623 "COMBINATORIAL"
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282309 "CHEMISTRY"
5609 "CHEMISTRIES"
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1615855 "CHEM"
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L7 11982 L6 AND COMBINATION THERAPY OR "E1 0 1 COMBINA
      TION/CT" OR "COMBINATION THERAPY" OR "E4 0 1

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COMBINATIONS/CT" OR "E7 3888 9 COMBINATORIAL CHEMI
STRY/CT" OR "E4 0 1 COMBINATIONS/CT"

=> d his

(FILE 'HOME' ENTERED AT 15:04:54 ON 03 MAY 2007)

FILE 'HCAPLUS' ENTERED AT 15:04:59 ON 03 MAY 2007

E WRIGHT G/AU 25

E WRIGHT GEORGE/AU 25

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L2 23 S (E26 OR E27 OR E28 OR E29 OR E30 OR E31 OR E32)
L3 611 S L1 OR L2
L4 19 S L3 AND HERPES
L5 1 S L4 AND COMBINAT?

FILE 'STNGUIDE' ENTERED AT 15:08:39 ON 03 MAY 2007

FILE 'HCAPLUS' ENTERED AT 15:08:55 ON 03 MAY 2007

E HERPES+ALL/CT

L6 26188 S (HERPES OR "HERPES" OR "INFECTION" (L) "HERPES" OR "SKIN, DIS
E COMBINATION THERAPY+ALL/CT
L7 11982 S L6 AND COMBINATION THERAPY OR "E1 0 1 COMB

=> s (combination therapy OR "E1 0 1 COMBINATION/CT" OR "COMBINATION
THERAPY" OR "E4 0 1 COMBINATIONS/CT")

504026 COMBINATION

116308 COMBINATIONS

594825 COMBINATION

(COMBINATION OR COMBINATIONS)

312210 THERAPY

28032 THERAPIES

327271 THERAPY

(THERAPY OR THERAPIES)

11979 COMBINATION THERAPY

(COMBINATION(W) THERAPY)

38843 "E1"

5595846 "0"

9117716 "1"

504026 "COMBINATION"

116308 "COMBINATIONS"

594825 "COMBINATION"

("COMBINATION" OR "COMBINATIONS")

27808 "CT"

1385 "CTS"

28972 "CT"

("CT" OR "CTS")

0 "E1 0 1 COMBINATION/CT"

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504026 "COMBINATION"

116308 "COMBINATIONS"

594825 "COMBINATION"

("COMBINATION" OR "COMBINATIONS")

312210 "THERAPY"

28032 "THERAPIES"

327271 "THERAPY"

("THERAPY" OR "THERAPIES")

11982 "COMBINATION THERAPY"

("COMBINATION" (W) "THERAPY")

6390 "E4"

5595846 "0"

9117716 "1"

116308 "COMBINATIONS"

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 1385 "CTS"
 28972 "CT"

("CT" OR "CTS")

0 "E4" 0 1 COMBINATIONS/CT"

("E4" (W) "0" (W) "1" (W) "COMBINATIONS" (W) "CT")

L8 11982 (COMBINATION THERAPY OR "E1" 0 1 COMBINATION/CT
 " OR "COMBINATION THERAPY" OR "E4" 0 1 COMBINAT
 IONS/CT")

=> s combination therapy

504026 COMBINATION

116308 COMBINATIONS

594825 COMBINATION

(COMBINATION OR COMBINATIONS)

312210 THERAPY

28032 THERAPIES

327271 THERAPY

(THERAPY OR THERAPIES)

L9 11979 COMBINATION THERAPY

(COMBINATION (W) THERAPY)

=> s l9 and l6

L10 114 L9 AND L6

=> s l10 and kinase

289515 KINASE

55897 KINASES

298609 KINASE

(KINASE OR KINASES)

L11 31 L10 AND KINASE

=> s l0 and cidofovir

3124 L0

684 CIDOFOVIR

L12 0 L0 AND CIDOFOVIR

=> s l10 and cidofovir

76 LL0

684 CIDOFOVIR

L13 0 LL0 AND CIDOFOVIR

=> s l10 and cidofovir

684 CIDOFOVIR

L14 5 L10 AND CIDOFOVIR

=> d l14 ibib abs 1-5

L14 ANSWER 1 OF 5 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2007:217656 HCAPLUS <<LOGINID::20070503>>

DOCUMENT NUMBER: 146:350372

TITLE: Acyclic nucleoside phosphonates: Past, present and future

AUTHOR(S): De Clercq, E.

CORPORATE SOURCE: Rega Institute for Medical Research, K.U. Leuven, Louvain, B-3000, Belg.

SOURCE: Biochemical Pharmacology (2007), 73(7), 911-922
 CODEN: BCPCA6; ISSN: 0006-2952

PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. Twenty years following the description of the broad-spectrum antiviral activity of S-9-(3-hydroxy-2-phosphonylmethoxypropyl)adenine the

acyclic nucleoside phosphonates have acquired a prominent therapeutic position: (i) cidofovir in the treatment of papilloma-, herpes-, adeno- and poxvirus infections, (ii) adefovir in the treatment of chronic hepatitis B virus (HBV) infections, and (iii) tenofovir in the treatment of human immunodeficiency virus (HIV) infections (AIDS). Although formally approved only for the treatment of human cytomegalovirus (HCMV) retinitis in AIDS patients, cidofovir has been used successfully in the treatment of various other DNA virus infections, particularly human papilloma virus (HPV)-associated lesions. Adefovir dipivoxil has become a standard therapy for HBV infections, especially when resistant to lamivudine. Tenofovir disoproxil fumarate (TDF) is the corner stone of the triple-drug (TDF, emtricitabine, and efavirenz) combination therapy for AIDS, and TDF, alone or combined with emtricitabine may in the future evolve to the standard therapy of hepatitis B. Guided by the results obtained with tenofovir in the prevention of parenteral, intravaginal and perinatal infections with simian immunodeficiency virus in monkeys, and the safety profile gathered with TDF in humans with AIDS over the past 5 years since TDF was licensed for clin. use, it should be further pursued for the pre- and post-exposure prophylaxis of HIV infections in humans. Meanwhile, new classes of both acyclic (i.e. PMPO-DAPy, PMEO-DAPy, HPMPO-DAPy) and cyclic nucleoside phosphonates (i.e. PMDTA, PMDTT, GS9148) have been accredited with an antiviral potency and selectivity similar to those of cidofovir, adefovir and/or tenofovir.

REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 2 OF 5 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:99157 HCAPLUS <<LOGINID::20070503>>
DOCUMENT NUMBER: 142:170033
TITLE: Methods and compositions for the treatment or prevention of human immunodeficiency virus and related conditions using cyclooxygenase-2 selective inhibitors and antiviral agents
INVENTOR(S): Maziasz, Timothy
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 172 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005026902	A1	20050203	US 2004-769485	20040130
PRIORITY APPLN. INFO.:			US 2003-443910P	P 20030131
OTHER SOURCE(S):	MARPAT 142:170033			

AB The present invention provides compns. and methods for the treatment of human immunodeficiency virus (HIV) infection as well as HIV associated diseases and related disorders. More particularly, the invention provides a combination therapy for the treatment of HIV infection as well as HIV associated diseases and related disorders comprising the administration to a subject of an anti-human immunodeficiency virus agent in combination with a cyclooxygenase-2 selective inhibitor or an isomer or a pharmaceutically acceptable salt, ester, or prodrug thereof.

L14 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:857189 HCAPLUS <<LOGINID::20070503>>
DOCUMENT NUMBER: 141:325791
TITLE: Treatment and prevention of otic disorders with cyclooxygenase 2 (COX-2) inhibitors alone or in combination with otic agents

INVENTOR(S): Seibert, Karen
 PATENT ASSIGNEE(S): Pharmacia Corporation, USA
 SOURCE: U.S. Pat. Appl. Publ., 60 pp.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004204471	A1	20041014	US 2004-772760	20040204
WO 2004093870	A1	20041104	WO 2004-US2990	20040204
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: US 2003-456286P P 20030320

AB A method for preventing or treating otic disorders and otic disorder-related complications in a subject involves a monotherapy with a COX-2 inhibitor or a combination therapy with a COX-2 inhibitor and an otic agent. Also described are therapeutic compns. comprising a COX-2 inhibitor and an otic agent. Pharmaceutical compns. and kits for implementing the method are also described.

L14 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:550871 HCAPLUS <<LOGINID::20070503>>
 DOCUMENT NUMBER: 141:82300
 TITLE: Methods and compositions for the treatment of herpes virus infections using cyclooxygenase-2 selective inhibitors or cyclooxygenase-2 inhibitors in combination with antiviral agents

INVENTOR(S): Maziasz, Timothy
 PATENT ASSIGNEE(S): Pharmacia Corporation, USA
 SOURCE: PCT Int. Appl., 155 pp.
 CODEN: PIXXD2

DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004056349	A2	20040708	WO 2003-US40615	20031219
WO 2004056349	A3	20040826		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2510445	A1	20040708	CA 2003-2510445	20031219

AU 2003297397	A1	20040714	AU 2003-297397	20031219
AU 2003297397	A2	20050707		
US 2004157848	A1	20040812	US 2003-742400	20031219
EP 1572186	A2	20050914	EP 2003-813794	20031219
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003017539	A	20051122	BR 2003-17539	20031219
CN 1726018	A	20060125	CN 2003-80106066	20031219
JP 2006512367	T	20060413	JP 2004-562315	20031219
PRIORITY APPLN. INFO.:			US 2002-435392P	P 20021219
			WO 2003-US40615	W 20031219

OTHER SOURCE(S): MARPAT 141:82300

AB The present invention provides compns. and methods for the treatment of herpes virus infections. In one aspect, the invention provides a combination therapy for treating a herpes virus infection comprising the administration to a subject of an anti-herpes virus agent in combination with a cyclooxygenase-2 selective inhibitor. In another aspect, the invention provides a mono therapy for treating a herpes virus infection comprising administering a cyclooxygenase-2 selective inhibitor to a subject.

L14 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:185447 HCAPLUS <<LOGINID::20070503>>

DOCUMENT NUMBER: 130:261355

TITLE: Topical antiviral agents for herpes simplex virus infections

AUTHOR(S): Hamuy, Ronnit; Berman, Brian

CORPORATE SOURCE: Department of Dermatology and Cutaneous Surgery, University of Miami School of Medicine, Miami, FL, USA

SOURCE: Drugs of Today (1998), 34(12), 1013-1025

CODEN: MDACAP; ISSN: 0025-7656

PUBLISHER: Prous Science

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review with 53 refs. Several antiviral agents against herpes simplex virus (HSV) infection have been clin. studied. Earlier therapies include glutaraldehyde, povidone-iodine, butylated hydroxytoluene and ether. Nucleoside analogs have been tested for efficacy in HSV. Although acyclovir and adenine arabinoside have shown minimal therapeutic benefit, cidofovir has been successful in the treatment of acyclovir-resistant strains of HSV, and idoxuridine 1% in DMSO, edoxudine and penciclovir have significant clin. benefit against HSV. Interferon- α has shown synergism with other anti-HSV drugs such as caffeine, trifluorothymidine, DMSO and nonoxynol-9, and ascorbic acid shows promising effects against HSV. Using a vehicle that enhances skin penetration of a drug or further exploring combination therapy may result in efficacious treatment of HSV. Vaccination or gene therapy may also prove beneficial in future studies.

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Katakura, Tatsushi / Kobayashi, Makiko / Fujita, Kazuhiko / Herndon, David N / Pollard, Richard B / Suzuki, Fujio, *Clinical immunology (Orlando, Fla.)*, Dec 2002

...patients, have been described as inhibitors for the type 1 T cell generation. Therefore, the antiviral effects of **combination therapy** with a type 1 T cell inducer [interleukin (IL)-12] and a type 2 T cell inhibitor [soluble IL-4 receptor (sIL-4R...

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Bajwa, Z H / Ho, C C, *Geriatrics*, Dec 2001

...diminished libido. Management of zoster-related pain should begin as soon as possible after the onset of symptoms. **Combination therapy**--including antiviral, antidepressant, corticosteroid, opioid, and topical agents--provides the most effective...

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Schmitt, Barbara / Wendtner, Clemens M / Bergmann, Manuela / Busch, Raymonde / Franke, Astrid / Pasold, Rita / Schlag, Rudolf / (...) / Hallek, Michael, *Clinical lymphoma*, Jun 2002

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...95300-3 Elsevier Science (USA) Regular Article A **Combination Therapy** Using IL-12 and Soluble IL-4 Receptor on Herpes...generation. Therefore, the antiviral effects of **combination therapy** with a type 1 T cell inducer [interleukin (IL...

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Meyding-Lamadé, Uta K / Oberlinner, Christoph / Rau, Philipp R / Seyfer, Sonja / Heiland, Sabine / Sellner, Johann / Wildemann, Brigitte T / Lamadé, Wolfram R, *Journal of neurovirology*, Feb 2003
Despite early antiviral treatment, herpes simplex virus encephalitis (HSVE) still remains a life-threatening sporadic disease with high mortality and morbidity. In patients and in experimental disease, chronic progressive magnetic resonance imaging (MRI) ...

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- ☐ 6. Effect of a combination therapy between IL-12 and soluble IL-4 receptor (sIL-4R) on Candida albicans and herpes simplex virus type I infections in thermally injured mice.
Kobayashi, Makiko / Takahashi, Hitoshi / Herndon, David N / Pollard, Richard B / Suzuki, Fujio, *Canadian journal of microbiology*, Oct 2002
The effectiveness of a combination using IL-12 and soluble IL-4 receptor (sIL-4R) to treat severe infections of herpes simplex virus type 1 (HSV-1) and Candida albicans in thermally injured mice was investigated. Although sIL-4R decreased burn-associated ...

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Chahlavi, A / Todo, T / Martuza, R L / Rabkin, S D, *Neoplasia (New York, N.Y.)*, Jun 1999
...therapeutic effects of cisplatin and G207 in vivo were independent. However, in cisplatin-sensitive tumors (UMSCC-38), **combination therapy** resulted in 100% cures in contrast to 42% with G207 or 14% with cisplatin alone. We conclude that G207 should...

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Stanwick, Trevor L. / Schinazi, Raymond F. / Campbell, Donald E. / Nahmias, Andre J., *Antimicrobial Agents and Chemotherapy*, Dec 2003

Acyclovir and human interferon displayed an additive to synergistic effect in reducing the number of herpes simplex viral plaque-forming units in Vero cells, suggesting a therapeutic potential for such **combination therapy**.

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...preparation of 348U87 (3%) in combination with acyclovir (5%) in an open-labelled study. Transient improvement with **combination therapy** occurred frequently; however, target lesions reepithelialized completely in only 1 of 10 patients. Termination...

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Cave, William / Pandey, Prativa / Chatterjee, Santanu, *Journal of travel medicine : official publication of the International Society of Travel Medicine and the Asia Pacific Travel Health Association*, Sep 2003

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...BILD 1633 SE also significantly decreased the lesions caused by HSV-1 dlsptk infection (28 to 51% AUC reduction). **Combination therapy** with topical BILD 1633 SE (5%) and ACV in drinking water (5 mg/ml) produced an antiviral effect against HSV-1...

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...the results of clinical trials have been disappointing. To improve the performance of tk/GCV therapy, we tried **combination therapy** designed to enhance its cytotoxic effects by introducing genes that induce apoptosis of the tumor cells through...

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Kobayashi, Makiko / Takahashi, Hitoshi / Herndon, David N / Pollard, Richard B / Suzuki, Fujio, *Burns : journal of the International Society for Burn Injuries*, Feb 2003
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Jef / Neyts, Johan / De Clercq, Erik / Herdewijn, Piet, *Antiviral chemistry & chemotherapy*, Jan 2003

Current standard therapy for the treatment of chronic infections with hepatitis C virus consists of **combination therapy** with (pegylated) interferon-alpha and ribavirin. 1,5-Anhydrohexitol nucleoside analogues are constrained congeners known to mimic...

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Blank, Stephanie V / Rubin, Stephen C / Coukos, George / Amin, Kunjlata M / Albelda, Steven M / Molnar-Kimber, Katherine L, *Human gene therapy*, Mar 2002

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***Antiviral Research*, Jan 1988**

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Schmutzhard, E, *Journal of neurology*, Jun 2001

...Nevertheless, if other causes for the clinical/neurological syndrome of peripheral facial palsy have been excluded, a **combination therapy** with acyclovir plus prednisone seems to be indicated in a patient with Bell's palsy.

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Kuriyama, S / Sakamoto, T / Masui, K / Nakatani, T / Tominaga, K / Kikukawa, M / Yoshikawa, M / (...) / Tsujii, T, *International journal of cancer. Journal international du cancer*, May 1997

The efficacy of expression of the herpes simplex virus **thymidine kinase** (HSV-tk) gene under the transcriptional control of the...wild-type HCC cells. Our results indicate the feasibility of **combination therapy** with the HSV-tk gene and ganciclovir for the treatment...

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...simplex virus **thymidine kinase** gene (HSV-tk...GCV-mediated killing, **combination therapy** continued to...potential benefit of **combination therapy** in patients...simplex virus **thymidine kinase** gene (HSV-tk...by endogenous **kinases**. The triple...benefits of **combination therapy**.
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...requires initial phosphorylation by viral **thymidine kinase**. The remaining two phosphorylation...activation via phosphorylation by viral **thymidine kinase** * Also binds with 30 to 50 times more...DNA polymerase * Depends on viral **thymidine kinase** for initial phosphorylation, then...

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Ellis, M N / Lobe, D C / Spector, T, *Antimicrobial agents and chemotherapy*, Oct 1989
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...improve on efficacy include incorporation of cytotoxic genes, such as tumor necrosis factor in Ad.DF3-E1, and herpesvirus **thymidine kinase** in E1B-deleted adenovirus [36,37] . Such alterations have been shown to promote more effective and sustained tumor regression...
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...play an attractive role in **combination therapy**. In this study, the effect...particularly sensitive to TCS. **Combination therapy** using more than one anti-viral...phosphorylated by HSV-specific **thymidine kinase** [7] . It is therefore active...
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...alone [14] , if the second drug has a different mechanism of activity. ACV selectively inhibits herpes viruses having a **thymidine kinase** (TK). The viral TK activates the drug by phosphorylation to a monophosphate and this is subsequently converted by cellular...
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Oh, K.-W. / Lee, C.-K. / Kim, Y.-S. / Eo, S.-K. / Han, S.-S., *Journal of Ethnopharmacology*, Sep 2000
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Lobe, D C / Spector, T / Ellis, M N, *Antiviral research*, Feb 1991

Combination therapy with A1110U, an inactivator of the...mice infected with an ACV-resistant **thymidine kinase**-deficient mutant and an ACV-resistant TK-altered mutant HSV-1 isolated. **Combination therapy** was very effective in reducing lesion...

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Safrin, S / Schacker, T / Delehanty, J / Hill, E / Corey, L, *Journal of medical virology*, Jan 1993

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